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ANNALS OF SURGERY

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PRIMARY, SOLITARY LYMPHOID TUMORS OF THE GASTRO-INTESTINAL TRACT

SHIELDS WARREN, M.D., AND C. R. LULENSKI, M.D.

BOSTON, MASS.

FROM THE LABORATORIES OF PATHOLOGY OF THE COLLIS P. HUNTINGTON MEMORIAL HOSPITAL, NEW ENGLAND DEACONESS AND PONDVILLE HOSPITALS, AND THE DEPARTMENT OF PATHOLOGY, HARVARD MEDICAL SCHOOL, BOSTON, MASS.

THE DISTINCTION between local and generalized forms of lymphoid growths is not widely recognized. In the present communication we propose to discuss the primary, solitary lymphoid tumors of the gastro-intestinal tract.*

The publication within the last few years of studies[1, 2, 3] on numbers of gastro-intestinal lymphoid tumors has been most helpful in emphasizing the importance of this tumor and clarifying many of its growth characteristics. However, the distinction between solitary and generalized tumors has not often been made and there has been little discussion of the relative importance and behavior of the different histologic types. Lesions of the stomach have been stressed more than those occurring in the intestine.

Among 3,132 malignant tumors of the gastro-intestinal tract (chiefly surgically removed) studied in our laboratories, there are 28 (0.9 per cent) cases of solitary lymphoid tumors.† We have discarded from our series several other cases originally diagnosed as lymphoid tumor of the gastro-intestinal tract, concerning which there was some doubt as to the classification when they were reviewed.

Pathology.—Because of the present incomplete knowledge of the pathology of tumors of lymphatic tissue and the consequent confusion of terms, we have adopted the term lymphoid tumors to indicate the group of primary tumors originating from the cells of lymphatic tissue.

* We have included one case of lymphoma of the stomach in which there were multiple nodules of the stomach, grossly distinct, but probably representing a single tumor.

† We are indebted to the surgical staffs of the Huntington, Pondville, and Deaconess Hospitals for clinical data.

The histopathology of lymphoid tumors of the gastro-intestinal tract does not differ from those of lymph nodes. The absence of uniform terminology impels us to give a brief explanation of our classification.

We recognize four types of lymphoid tumors: Malignant lymphoma; Hodgkin's disease; lymphosarcoma; and reticulum cell sarcoma. All but the last are represented in our series. Malignant lymphoma is composed of quite well-differentiated medium and small lymphocytes, with usually few mitoses. This must be differentiated from the rare benign lymphoma which appears to be a true noninvasive tumor of lymph nodes and may occur as an isolated nodule in the intestine, localized, usually, in the submucosa and presenting a picture quite distinct from hyperplasia.

Hodgkin's disease presents a very variable picture and may be characterized by several or all of the following: Sternberg cells; pleomorphism; eosinophilia; necrosis; and fibrosis. In disease of long duration, fibrosis is sometimes the outstanding feature. Sternberg cells may be so large and numerous as to suggest an undifferentiated carcinoma.

Lymphosarcoma is a rapidly growing tumor, the cells relatively immature, quite uniformly large and pale, with numerous mitotic figures. Many of the cells resemble large lymphocytes and lymphoblasts. Some of them appear to be reticulum cells. Ignorance of the exact nature of these cells has given rise to much controversy. The tendency now is to consider most of these tumors of reticulum cell origin. We believe true reticulum cell sarcoma to be extremely rare, although proliferation of reticulum cells is often present in all forms of lymphoid tumors. Tumors that would be called reticulum cell sarcoma by some pathologists are grouped in our series as lymphosarcoma. Ewing[4] believes that some lymphosarcomata arise from reticulum cells, others from lymphocytes, and intimates that lymphosarcoma differs in behavior depending upon whether it arises from lymphoid cells or reticulum cells. So far as we know, there are no clinical grounds for distinguishing between lymphosarcoma and reticulum cell sarcoma. We should like to take issue with the concept that reticulum cell sarcoma is more resistant to radiation than other forms of lymphoblastoma. Of two authorities for this statement, one[5] gives no supportive evidence and the other[6] presents cases which are at best incomplete.

The 28 tumors presented in this paper are classified as follows: thirteen Hodgkin's disease, ten lymphosarcoma, five malignant lymphoma. Fourteen of the tumors are of the stomach, eight of the large intestine, and six of the small intestine. In 23 of these cases, the tumor was solitary with no evidence of metastasis in any other part, either local or distant; five cases had adjacent lymph node involvement.

The age and sex differences are not significant. The median age at the time of first examination was 53 years, with a range from 20 to 75 years. The ratio of males to females was 9:5—a preponderance of males over females which is present in all forms of lymphoblastoma and of gastro-intestinal

malignancy as well, and probably of no significance. We will consider the tumors of different parts of the gastro-intestinal tract separately.

TABLE I

STATISTICAL SYNOPSIS OF THE SITES OF TUMORS OF THE GASTRO-INTESTINAL TRACT

	Malignant Lesions	Primary, Solitary Lymphoid Tumors	Percentage	Hodgkin's Disease	Lymphosarcoma	Malignant Lymphoma
Stomach	569	14	2.5	6	6	2
Small intestine	53	6	11.3	4	1	1
Large intestine	2,510	8	0.3	3	3	2
Totals	3,132	28	0.9	13	10	5

TUMORS OF THE STOMACH

There are 14 cases of lymphoid tumors of the stomach, on 13 of which we have fairly complete data. Most individuals had rather general complaints. Half of the cases presented one or more of the following symptoms: Indigestion; anorexia; nausea; and vomiting. Three cases, presenting marked anemia, weight loss and blood in stools or gastric contents when first seen, died two weeks, one year, and three years, respectively, following operation. Total acidity and free HCl were slightly low in four out of six cases. Occult blood was demonstrated in gastric contents in three of six cases, and in one case a tumor, measuring 15 cm., was accompanied by marked anemia and blood in stools; the patient died two weeks after operation.

Roentgenologic examination led to the diagnosis of cancer in three cases; malignancy in four others; and benign ulcer in two cases. In one, the roentgenographic picture was interpreted as compatible with gastritis, lymphoid tumor or carcinoma. A gastroscopic examination (the only one performed upon any of these patients) was unsatisfactory. Celiotomy was performed in each case, and resection of the tumor in ten; two cases were inoperable. A biopsy was taken from each of these two tumors. A total gastrectomy was performed in one case with extensive tumor. Postoperative irradiation was given in three cases.

All of the tumors were large; half of them were over 5 cm., and three of these were over 10 cm.; the smallest was 2 cm. in greatest diameter. Six of the tumors involved, primarily, the lesser curvature, and two of them the greater curvature. Although many of the tumors involved a large part of the stomach, the proximal end was less frequently involved than the distal. Two of the tumors extended beyond the pylorus into the duodenum. Three of the tumors showed a slight degree of ulceration. Two tumors had ulcers 2 cm. in diameter, and three tumors had large ulcers 4 cm., or more, in diameter.

In 13 cases, the regional lymph nodes were described as enlarged. In only four of these was there histologic proof of metastasis. In two cases, the tumor had extended beyond the limits of the stomach into adjacent omentum, and in one other case part of the wall had been completely destroyed by necrotic tumor.

Seven of the 14 cases are dead, exitus occurring within a year following treatment in all but one case, in which an interval of three years elapsed between operation and death. Three of these were inoperable. A fourth case died one year after subtotal gastrectomy. The tumor had perforated the

FIG. 1.

FIG. 2.

FIG. 1.—Stomach—Hodgkin's disease; diffuse type: Male, age 57. Living three years.
FIG. 2.—Small intestine—malignant lymphoma; diffuse infiltration: Male, age 45. Living six years.

stomach wall and extended into the gastrocolic ligament at the time of operation, and was obviously not entirely removed. Death in the fifth case, a year after operation, may also have resulted from extensive tumor since this is the only example we have of multiple nodules of lymphoid tumor in the stomach.

However, the serosal coat was smooth and lymph nodes negative at the time of operation. No autopsy was performed. The cause of death in the sixth case, a male 75 years of age, dying six months following operation, is rather obscure, as the tumor, while large, was of mature cell type and low histologic malignancy, with no metastasis at the time of operation. The tumor was supposedly present at death, though this was not confirmed by autopsy. The

FIG. 3.—Colon—Hodgkin's disease; discrete type: Male, age 59. Died one and one-half years after first being seen.

seventh death was a male, 49 years old, who lived three years after excision of a rather extensive Hodgkin's disease without known secondary growths. The status of the tumor at death is not known.

It is worth noting that the tumors in all seven cases were solitary, without secondary distant deposits, and that, although disease was supposedly present at death in five cases, there were only two autopsies, and the cause of death in the other cases is not clear. The two autopsies showed the tumor still localized in the region of the stomach with no secondary deposits.

There are six cases still alive, and five of them without evidence of disease, one, two, three, four and nine years, respectively. One patient is living with disease a year after subtotal gastrectomy. Another patient had a tumor of the lesser curvature and posterior wall (10x7 cm.) resected four years ago, at the age of 72 years. There was no lymph node involvement at that time, but postoperative radiation was given (1,200 r. through two epigastric portals). Two years later, multiple lesions were found in the lungs which suggested tumor. There was also evidence of recurrence in the intestine. In November, 1938, six spray, high voltage roentgen ray treatments, of 30 r. each, were given to the chest and to the left side of the abdomen. The patient is alive four years following excision of the tumor, and two years since the last roentgen ray treatment. There is no definite evidence of disease at present. One patient, having had a subtotal gastrectomy two years ago, is lost.

TUMORS OF THE SMALL INTESTINE

There are six cases of lymphoid tumors of the small intestine; three located in the ileum, one in the jejunum, and two in unspecified locations. The symptoms were of little diagnostic import. All of the tumors were invasive, and the lumen tended to be narrowed rather than dilated. One of the patients with a lobulated tumor, apparently originating at the mesenteric attachment of the ileum, is living without disease six years later. The tumors were large, measuring 5, 5, 7, 9, 15, and 18 cm. in greatest diameters. Two of the largest tumors were deeply ulcerated. Three of the tumors had extended slightly into the mesentery. There were no lymph node metastases of any tumors at the time of operation.

Three cases were resected, and are living two, two, and six years after operation, without evidence of disease. Tumors in these cases were diagnosed Hodgkin's disease, lymphosarcoma, and malignant lymphoma, respectively. One untreated case, seen first a few weeks before death, was extremely emaciated at that time and presented a large tumor in the left upper quadrant. Roentgenograms were negative. At autopsy, the tumor mass proved to be Hodgkin's type, infiltrating two adjacent loops of jejunum and forming a single, hollow, honeycombed mass with no secondary deposits in other tissue. One patient died of peritonitis two days after resection of a tumor of the ileum (Hodgkin's disease) infiltrating 7 cm. of the length of the wall. One patient with Hodgkin's disease of the ileum is lost.

TUMORS OF THE LARGE INTESTINE

There are eight patients with lymphoid tumor in the colon. There is only one female in the group. Three of the tumors were polypoid, arising in the rectum; one was located at the hepatic flexure; one involved an unspecified portion of intestine and had extended into the mesocolon; three tumors were located in the cecum; two of them large and invading adjacent tissue, and the third lobulated.

The tumors were much smaller than those in the stomach and small intestine, the largest being 8 cm., two others 5 cm. and the others smaller.

A history of clinical symptoms was available in only three cases. One patient, a male, 59 years of age, had had symptoms for three months; occasional nausea, rare vomiting, anorexia, and lately anemia, weakness, progressive weight loss (25 lbs.), with constipation and recent obstipation. The tumor was firm, lobulated, annular, 5 cm. in diameter, with no ulceration. There was no extension into the serosa. Adjacent lymph nodes were involved by tumor. An intussusception of the ileum through the valve had occurred. The patient died two years later. No autopsy was performed but the tumor was said to be present. Another patient, a 23-year-old male, with lymphoid tumor of the cecum, had had mild symptoms for one year; nausea and occasional vomiting, with right lower quadrant pain, and a palpable mass for six months. At operation, at another hospital, a supposedly inoperable tumor of the cecum was found and a colostomy performed. The microscopic diagnosis

TABLE II

SUMMARY OF MORTALITY STATISTICS OF 28 CASES OF SOLITARY, PRIMARY LYMPHOID TUMORS OF THE GASTRO-INTESTINAL TRACT

	Hodgkin's Disease							Lymphosarcoma							Malignant Lymphoma												
				Years Living							Years Living							Years Living										
	No. of Cases	Followed	Surgery	No. of Cases	1–3	3–5	5+	No. of Cases	Followed	Surgery	No. of Cases	1–3	3–5	5+	No. of Cases	Followed	Surgery	No. of Cases	1–3	3–5	5+	Total No. of Cases	Total Followed	Total 1–3 Years	Total 3–5 Years	Total 5+ Years	Total Living‡
Stomach	6*	6	5	4	1	2	1	6	5†	4	1	1	–	–	2	2	2	1	1	–	–	14	13	3	2	1	6
Small intestine	4†	3	3	1	1	–	–	1	1	1	1	1	–	–	1	1	1	1	–	–	1	6	5	2	–	1	3
Large intestine	3	2	3	1	1	–	–	3	2	3	1	–	–	1	2	2	2	1	–	1	–	8	6	1	1	1	3
	—	—	—	–	–	–	–	—	–	–	–	–	–	–	–	–	–	–	–	–	–	—	—	–	–	–	—
Total	13	11	11	6	3	2	1	10	8	8	3	2	–	1	5	5	5	3	1	1	1	28	24	6	3	3	12

* One patient was inoperable, and was irradiated.

† One patient died—no therapy.

‡ Ten living, with no evidence of disease.

of a biopsy was "anaplastic carcinoma." A few months later the tumor was excised at Pondville Hospital, and it proved to be a lymphosarcoma. The tumor, 5 cm. in greatest diameter, appeared quite superficial, extending only slightly into the muscle. There was shallow ulceration. Enlarged regional lymph nodes, found at operation, were hyperplastic and not invaded by tumor. The patient is now alive and well, without disease five years after operation.

The third patient, on whom we have clinical data, had been treated for the past 11 years for duodenal ulcer. The immediate indication for investigation was the appearance of tarry stools for six months. A small polyp, 1 cm. in diameter, was excised from the internal rectal sphincter, followed by roentgenotherapy. The tumor was a typical lymphoid tumor, classified as "malignant lymphoma." The patient is living, without disease four years later. One other patient with polypoid tumor of the rectum (Hodgkin's disease), 3 cm. in diameter, is alive without disease two years after excision. The third case of polypoid tumor of the rectum (lymphosarcoma), 3 cm. in diameter, is lost. Another case is lost, that of lymphoid tumor of the hepatic flexure (Hodgkin's disease), measuring 8 cm. in diameter. The last case was a large (size not known), ulcerated, annular tumor o fthe cecum (lymphosarcoma). The patient, a 20-year-old male, died six months after operation, and the autopsy revealed a tumor extending through the retrocecal region into the right kidney and invading the pancreas and peripancreatic nodes.

Aside from two patients with polypoid lymphoid tumors of the rectum, there is only one patient known to be alive; this patient is without disease five years after right colectomy.

Discussion.—The foregoing statistics indicate that neither the type of lymphoid tumor nor the location causes any significant variation from the average prognosis. The average survival was 2.5 years. One patient has been living over a year, with disease present. Ten patients are alive for periods of one to nine years postoperatively, with no evidence of disease. Among these there are three five-year cures.

From a review of this group of 28 cases, few conclusions are possible which would help in establishing the clinical diagnosis of lymphoid tumors. But there are a few considerations which suggest that a given tumor may be of lymphoid type. One of the most important is the relatively good condition of a patient presenting a large tumor. Patients with carcinomata as extensive as the majority of the solitary lymphoid tumors, usually present a striking picture of debility. This is particularly true of lymphoid tumors of the stomach. Those in the intestine may cause early, general symptoms related to anemia. In the stomach, the diagnosis must be suspected whenever a large tumor is accompanied by ulcer-like symptoms and vomiting of nonobstructive type. Hematemesis from a tumor in a young person may also be suggestive. In only one of our cases was lymphoid tumor considered in the differential diagnosis, with carcinoma and gastritis as alternatives. Two of our lymphoid tumors of the stomach were thought to be simple ulcers, from

the roentgenograms. There are no roentgenologic features diagnostic of lymphoid tumors and, as a rule, roentgenograms are helpful only insofar as they point to a tumor. But certain aspects are pertinent. In a typical instance, the stomach shows a slightly raised tumor, neither annular nor constricting, with a central, superficial ulcer. Large hypertrophic rugae in the stomach, either with or without a filling defect, may suggest the disease. The small intestine usually shows an encircling growth which may cause either enlargement or diminution of the lumen in the affected part. Special technics are useful in assuring a more complete study of small intestine than is ordinarily attainable.[7]

Gross Pathology.—The gross appearance, on the other hand, is often quite well-defined. Lymphoid tumors, in whatever part of the body they may occur, grow along lines of least resistance, to an extent not seen in other malignant growths. As a result, tissues are separated along cleavage planes, thus accentuating different structures, such as mucosa, submucosa, and muscularis, and producing fairly uniform, diffuse enlargement of the part invaded. It is only later, when the growth is more exuberant, and normal barriers are broken down by pressure of the proliferating tumor cells, that structures are obliterated and necrosis occurs. There are two main types of growth seen in lymphoid tumors: (1) Diffuse growth involving a large part of an organ, causing fairly uniform, diffuse thickening, sometimes with discrete tumors here and there, with or without ulceration; and (2) a large solitary tumor, with usually deep ulceration or rather cavitation. Rarely, polypoid forms of the tumor are seen.

The serosa is not invaded or distorted by lymphoid tumor, except in rare cases when the tumor is very large. An extensive tumor, which does not greatly distort the organ or involve the serosa, is very likely to be of lymphoid nature.

Lymphoid tumors, usually, are succulent and more resilient than most carcinomata, although Hodgkin's disease may present a very firm, fibrous structure. They are rarely recognized when they are small, and when first observed are usually much larger than carcinomata.

Other lesions having gross features in common with lymphoid tumors are: Diffuse carcinoma simplex; leiomyoma and leiomyosarcoma; and a diffuse inflammatory change such as cicatrizing enteritis and syphilis of the stomach. Diffuse carcinoma simplex, fairly commonly seen in the stomach but rare in other parts of the intestinal tract, may cause a uniform thickening of the wall, separating without distorting the structural units in a manner similar to that of lymphoid tumors with the difference that this type of carcinoma produces a rigid, contracted organ, and is frequently mucus-secreting.

Most inflammatory conditions are easily distinguished from lymphoid tumors, but cicatrizing enteritis (regional ileitis) may cause a diffuse, uniform thickening without loss of structure. Diffuse gastritis, especially of syphilitic origin, may, similarly, be confusing to differentiate.

The large, globular, lymphoid tumors may resemble leiomyoma or leiomyosarcoma. The benign and malignant forms of smooth muscle tumors are rarely seen in the gastro-intestinal tract, but are somewhat more common in the stomach than elsewhere. They usually present as a discrete, rounded, resilient tumor, either intrinsic in the wall or pedunculated toward the mucous or serous surface. Even when the histologic structure is that of a fairly malignant tumor, the growth tends to be delimited rather than invasive. Necrosis and ulceration are the usual signs of malignancy and rapid growth. The lymphoid tumors, though expansile, do not often become pedunculated.

It is important to determine whether or not the tumor is part of a generalized disease. This is a more important problem in the small bowel, where secondary, lymphoid tumors are more commonly found. The most helpful consideration is the infrequency of secondary tumors in the small bowel without large metastases in either the mesenteric or retroperitoneal lymph nodes. Secondary lymphoid tumors are less common in the stomach and large bowel, and practically never reach the size of the usual primary, lymphoid tumor.

Treatment.—All of our cases were treated, primarily, by surgical excision, all but three being removed at operation; one of these was inoperable, the tumor was biopsied and irradiated. Two patients died without therapy, but biopsy was taken in one of these cases. Two cases of lymphoid tumors of the stomach received postoperative roentgenotherapy, and are living and well, without disease three and four years after treatment. Both were Hodgkin's type. Because of the uncertainty in the diagnosis of lymphoid tumors, either with or without biopsy, excision is the treatment to be preferred. Postoperative irradiation may be definitely beneficial for those tumors which cannot be completely removed. In the literature, there are reports of at least nine four-year cures by irradiation alone.[2, 8] This suggests that this therapy may assume greater importance in the future,[2, 9] in spite of certain dangers in radiation of tumors involving a hollow viscus.

Discussion.—Solitary, lymphoid tumors of the gastro-intestinal tract are of not infrequent occurrence and should be considered in differential diagnosis. It may be useful to compare these tumors with solitary, lymphoid tumors arising primarily in other regions. Lymphoid tumors of the skin, without evidence of lymph node or organ involvement, have long been recognized and often classified under the broad descriptive term of "mycosis fungoides."[10] These tumors in the skin may be the first manifestation and sole evidence of disease for many years. The majority of the patients that come to autopsy have similar tumors involving either lymph nodes or organs.

Lymphoid tumors of the bone of the reticulum cell type have been described with increasing frequency during the past ten years.[11] In cases reported by Parker and Jackson,[12] and in cases reported by Simmons,[13] secondary foci of tumor have developed in only a few cases after several years of observation.

Whether the tumor is in the skin, bone, or gastro-intestinal tract, the dis-

tinction must be made between the tumors which are primary and remain solitary for some time, and those in which the first evidence of disease happens to be a local process in these tissues, soon to be followed by generalized disease.

In studies of a small series of cases of solitary, lymphoid tumors, in skin, bone, or gastro-intestinal tract, one has the impression that these tumors have a relatively benign course in contrast to other forms of malignancy in the same locations, and as against generalized lymphoid tumors. Operative removal frequently results in cures for five to 15 years. But there are, as yet, too few reported cases for any volume of statistics to have accumulated from which one may draw conclusions. The average duration of life of our 28 primary lymphoblastomata of the gastro-intestinal tract is 2.5 years, comparable to three years, reported by Madding and Walters.[3] The life expectancy for generalized lymphoid tumors is two years, as reported by Nathanson.[14]

SUMMARY AND CONCLUSIONS

In a series of 3,132 malignant lesions of the gastro-intestinal tract there are 28 cases of primary, solitary lymphoid tumors, an incidence of 0.9 per cent.

The characteristics of these tumors have been considered from the point of view of clinical symptoms, treatment, and outcome, and the gross and microscopic pathology.

These tumors remain solitary for many years, and may reach a large size before causing disturbing symptoms.

Metastasis to regional lymph nodes and extension into adjacent tissue occur late in the disease, if at all.

The behavior of primary, solitary lymphoid tumors in the gastro-intestinal tract is not unlike that of similar tumors in bone and skin.

In this series, the prognosis for the solitary form is but little better than for generalized lymphoid tumors, but in many cases long survival periods and possibly complete cures have been obtained by adequate treatment.

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RUPTURE OF THE COLON BY COMPRESSED AIR

REPORT OF THREE CASES

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COMPRESSED AIR came into rather general use in industry at about the beginning of the twentieth century. In 1904, Stone[1] reported a fatal case of rupture of the bowel caused by compressed air introduced per rectum from a machine which was pumped by hand. In 1908, Petren[2] wrote about a case of fatal rupture of the esophagus from accidental oral insufflation. In 1911, Andrews[3] reported a case of pneumatic rupture of the sigmoid colon which recovered following resection of the injured loop. He also discussed the subject quite completely and recorded 15 other cases collected by correspondence and from law reports. Later in the same year, Lenormant[4] reviewed the previous papers and discussed the subject editorially in the Presse Medicale, of Paris. The following year, Cotton[5] reported the recovery of a case of perforation of the ascending colon—he established a temporary colostomy at the site of the perforation and repaired several rents in the serous and muscular coats of other portions of the colon. In 1914, Bendixen and Blything[6] reported another recovery—a case of pneumatic rupture of the transverse colon, and gave brief notes on seven collected cases which were fatal. Buchbinder[7] reported a fatal case in 1921.

There have been a number of more recent publications on this subject. Table I gives a brief summary of cases of complete rupture of the bowel from compressed air that we have found in a rather thorough search of the literature.* Hays[13] was apparently the first American author who was aware of Stone's original contribution. Burt[16] found that under experimental conditions the human colon bursts with only about 4 lbs. pressure, and that the serous and muscular coats tear first at about 3½ lbs. pressure. Table II summarizes cases of incomplete rupture of the bowel. These two tables, and our bibliography, are arranged according to dates of publication. Our three cases illustrate various degrees of severity of bowel injury from compressed air.

CASE REPORTS

Case 1.—Dr. James H. Lewis: Complete Rupture of Transverse Colon with Marked Abdominal Distention. H. Z., white, male, age 21, was admitted to the Moses Taylor

* Data on two cases of Fauquez (Burt[16]); one of Houzel (Burt[16]), and one of Semerikov[20] are not included.

TABLE I

PNEUMATIC BOWEL PERFORATION

No.	Author	Year	Age	Treatment: Pounds Pressure	Treatment: Operation	Treatment: Time After Injury	Site of Perforation	Result
1	Stone	1904	17	20	Yes	(trochar)	Sigmoid	Died
2	Andrews	1910		60	Yes	5 hrs.	Sigmoid	Recovered
3	(1) Fletcher	1907	36	70	Yes	4½ hrs.	Sigmoid	Recovered
4	(2) Tilney	1907	21	—	No		——	Died, third day
5	(3) (Currie)	1906	—	40–100	Yes	?	——	Died
6	(4) (Ballard)	1908	—	—	No		——	Died
7	(5) Boughton	1910	39	—	Yes		Sigmoid (3 places)	Recovered
8	(6) Stevens	1910	20	—	Yes	9 hrs.	Splenic flexure	Died
9	(7) Sherman	—	—	—	No		——	Died (autopsy)
10	(8) (Banquet)	—	25	—	No		Rectum (2 places)	Died (autopsy)
11	(9) (Kaseberg)	1908	22	—	No		Rectum	Died (autopsy)
12	(10) (Borgan)	1906	25	—	No		Rectum	Died (autopsy)
13	(11) (Jaworski)	1905	47	—	Yes		Sigmoid	Died (autopsy)
14	(13) Burry	1907	20	125	Yes		Colon (3 places)	Died (autopsy)
15	(15) Godfrey	1908	19	80	No		Upper end sigmoid	Died (autopsy)
16	Cotton	1912	—	—	Yes	3 hrs.	Ascending colon	Recovered
17	Bendixen & Blything	1912	20	100–125	Yes	2 hrs.	Transverse colon	Recovered
18	(1) (Orth)	1908	—	—	Yes		——	Died, 3 hrs.
19	(3) (Dagenais)	1906	15	—	Yes	4 days	Sigmoid	Died (autopsy)
20	(5) (Denney)	—	—	—	No		——	Died
21	(6) Groman	—	15	—	Yes	After trochar	Near cecum	Died
22	(7) Mecray	1913	17	10	No		Colon (8 places)	Died (autopsy)
23	Buchbinder	1920	—	85	Yes		Sigmoid (gangrene)	Died (autopsy)
24	Jean (1)	—	—	—	Yes	4 hrs.	Rectosigmoid junction	Recovered
25	(2)	—	—	—	Yes	2½ hrs.	Sigmoid	Recovered
26	Hailes	—	—	—	Yes	19 hrs.	Colon	Died
27	Sparkman	1922	—	—	Yes (centesis)	3 hrs.	Sigmoid	Recovered
28	Block & Weissman	1925	45	125	Yes	5½ hrs.	Sigmoid	Recovered
29	Hays	1923	30	95	Yes	1 hr. 50 min.	Rectum	Recovered
30	Patterson	1930	—	—	Yes		Hepatic flexure	Recovered
31	Burt (1)	—	49	2	Yes		Iliac (old colitis)	Died
32	(a) Shoudy	1927	—	—	Yes		Many	Recovered
33	(b) Shoudy	1916	—	—	No		——	Died
34	(c) Shoudy	1927	—	—	Yes		——	Recovered
35	(2) Moorehead	1928	37	—	Yes	25 hrs.	Sigmoid (3 places)	Recovered
36	Ide	1930	—	—	Yes	3 hrs.	Sigmoid	?
37	(1) L. F.	—	12	—	Yes		Rectum, sigmoid and descending colon	Died
38	(2)	—	—	—	Yes		Lower end of sigmoid	Died
39	(3)	—	—	—	No		——	Died
40	(4) C. R.	1920	—	—	No		——	Died
41	(5)	1918	16	—	?		——	Died
42	(6) Nilsson	1926	—	—	No		——	Died
43	(7)	1914	21	—	Yes		——	Died
44	(8)	—	—	—	No		——	Died
45	(10) Wainwright	—	—	90	Yes	6 hrs.	Loud explosion	Recovered
46	(11)	—	—	—	Yes		Sigmoid	Recovered
47	(12)	—	—	—	Yes (centesis)		——	Died, 5 hrs.
48	(13)	—	—	—	No		——	Died, 24 hrs.
49	(14)	—	—	—	No		——	Died
50	(15)	1936	—	—	No		——	Died
51	(16) Mr. P.	—	—	—	No		——	Died
52	(17) A. L.	—	—	—	?		Colon	Died

TABLE I (*Continued*)

No.	Author	Year	Age	Treatment: Pounds Pressure	Treatment: Operation	Treatment: Time After Injury	Site of Perforation	Result
53	(18)	1915	—	—	No		Rectum	Died, 3 hrs.
54	(19) J. H.	1915	—	—	?		——	Died
55	(20)	1920	—	—	?		Colon	Died, 8 days
56	(21)	1936	—	90	Yes		——	Died during operation
57	(23) Cereal.....	—	—	—	?		——	Died
58	(24)	—	—	—	?		Sigmoid	Died
59	(25)	—	—	—	?		——	Died
60	Ritchie.....	—	—	—	Yes	6 hrs.	Sigmoid	Recovered

TABLE II

PNEUMATIC BOWEL INJURY WITHOUT PERFORATION

No.	Author and Case Mark	Date	Age	Lbs. Air Pressure	Treatment	Pathology	Result
1	Andrews XII Kahlke	1906	20	—	Operation; 18 hrs.	Colon ruptured entire length, except for 1 or 2 narrow bands. Mucosa was not perforated.	Died
2	XIV Burry	1908	—	—	None	Insufflation with live steam.	Recovered
3	Bendixen & Blything (Orth)	1913	16	85	None	Returned to work shortly.	Recovered
4	(Kay)	1905	—	—	None	Recovery rapid and complete.	Recovered
5	Schwartz	1922	—	20–70	Operation; 6 hrs.	No perforation found but serous and muscular coats of large intestine were lacerated.	Recovered
6	Morris	1923	—	60–65	Operation	Mucosa bulged through 7-inch tears on each side of cecum. Sigmoid had a number of small tears, but mucosa not ruptured.	Recovered
7	Ide IX	1929	—	—	None	Not serious; returned to work in 10 days.	Recovered
8	XXII	—	—	—	None	Injuries minor. No disability.	Recovered
9	Neese	1936	42	75	Operation	Multiple areas of herniation of mucosa of descending colon and sigmoid—due to tearing of serous and muscular coats. No perforations.	Recovered

Hospital, April 1, 1915. He had collapsed immediately after air was released from a nozzle which was held against the seat of his trousers. At the time of admission he was in profound shock. Temperature, by mouth, 96° F., pulse 92, respirations 26. The abdomen was markedly distended; liver dulness to percussion was absent. The lower extremities were blue and cold. There was a protrusion at the anus, and prostatic secretion was noticed at the urinary meatus. A rectal tube was inserted but no air escaped. Vomitus was fecal.

Operation.—About two hours after the injury: Under general ether anesthesia, a midline incision above and below the umbilicus was made. The skin and underlying tissues retracted widely. When the peritoneum was opened there was a sudden deflation. The pelvis contained a brownish-red fluid. There were several tears through the serous and muscular coats of the transverse colon and in its midportion there was an opening through the mucous layer about one inch long. Both the ascending and descending colon had been loosened from the parietes in places; at the iliocecal junction there was an ecchymosis three inches in diameter. The small intestines contained air and the gallbladder was distended with air, being three and one-half inches long and one and one-half

inches in diameter. The perforation was sutured; the peritoneal cavity was sponged grossly clean; drains were inserted; and the wound was closed.

The postoperative course was stormy. A fecal fistula developed, which closed spontaneously. The patient left the hospital in good health 90 days after the accident.

Case 2.—Dr. James H. Lewis: Incomplete Ruptures of Rectum and Sigmoid Colon. J. B., white, male, age 40, was admitted to the Moses Taylor Hospital, August 6, 1916, complaining of abdominal pain and vomiting, which occurred immediately after his fellow workmen released the compressed air against his anus. Temperature 96.8° F., pulse 74, respirations 20. He seemed to be in great pain and was dazed. There was slight rigidity in both lower quadrants of the abdomen; but there was no bulging or distention.

Operation.—Six hours after injury: Under general ether anesthesia, an incision was made in the midline below the umbilicus. There was no noticeable escape of air when the peritoneum was opened. There were five tears in the serous and muscular coats of the sigmoid colon, and one of the rectum; but no perforation in the mucosa was discovered. These tears were sutured and the abdomen was closed. A rectal tube was inserted. The patient made an uneventful recovery and was discharged from the hospital 30 days after the injury.

Case 3.—Drs. Brown and Dwinelle: Complete Rupture of Sigmoid Colon, without Abdominal Distention. W. R., white, male, age 24, was admitted to the Moses Taylor Hospital, July 29, 1939. The patient had a tear along the seam of his trousers on the medial aspect of his thigh, into which a fellow workman, jokingly, had directed the compressed air jet. He felt some pain in the upper part of the abdomen and had to sit down because of weakness. In a few minutes he felt better, changed his clothes and walked to the dispensary. Temperature 99° F., pulse 88, respirations 20, blood pressure 120/84. At this time he had practically no pain. There was no distention of the abdomen; there was no rigidity, and only slight tenderness just above the symphysis pubis. There was no area of dulness to percussion in the region of the liver. A roentgenogram of the abdomen in the erect position showed air between the diaphragm and the liver (Fig. 1).

Operation.—Four hours after the injury: Under general ether anesthesia, a low left rectus incision was made. The peritoneum was opened beneath sterile saline solution; air bubbled out as soon as the peritoneum was incised. There was a little blood mixed with fecal material in the pelvis. An irregular stellate rupture about two inches long in the lower part of the sigmoid flexure was sutured with silk with considerable difficulty. A rectal tube was guided up past the site of injury; cigarette drains were placed on either side of the injured bowel; and the abdomen was closed in layers. A fecal fistula developed which closed spontaneously 24 days after the accident. The patient left the hospital in good health on the 58th day.

Pathogenesis.—This accident is not uncommon, because the public is not aware of the fact that a compressed air jet is a lethal weapon. All the victims were males, between the ages of 12 and 49. Many cases are due to pranks, but not all of them. Workmen should never dust off their clothes with compressed air.

The jets that are used in industry are usually said to have a pressure of from 50 to 100 lbs. or more. The nozzles are pipes one-quarter to one inch in diameter; sometimes the rubber hose is used without a nozzle. Usually one thinks of these jets in terms of experience with visible streams of water from a nozzle; but the gaseous jet differs in that it is elastic and expands in all directions, adapting itself to surroundings, bending and twisting and causing eddy currents.

Such an air jet enters the anus more readily than the examining finger or a proctoscope, as it passes through clothing and enters the bowel even when not accurately directed at the anus, as in Case 3. It has been suggested[3] that the thighs, buttocks and perineum form a funnel which delivers the stream of air to the anus. Gases under pressure pass through small apertures very rapidly. Compressed air has been known to enter a hangnail accidentally and produce signs suggestive of gas gangrene of the hand and forearm.

FIG. 1.—Case 3: Preoperative roentgenogram; sitting up. Shows gas beneath the diaphragm.

Rupture of the intestine perhaps depends more upon the suddenness of the pressure than upon its amount, for the bowel will expand enormously if given time to relax. Duval (quoted by Burt[16]) observed great dilatation of the colon in a deranged patient who inflated himself by means of a hand bicycle pump. Operation was performed in error, with a diagnosis of megacolon, and no abnormality was found.

Apparently the muscularis mucosae adapts itself more readily to sudden changes in tension than the outer muscular coats of the bowel. Rents in the muscle, usually along one of the longitudinal bands, with the underlying mucosa intact, have been observed in many cases. Case 2, and at least some of those listed in Table II, illustrate the occurrence of these incomplete lacerations without any associated complete perforation. The inner mucosal tube balloons out through the split outer muscular tube, like the "blow-out" of a pneumatic tire. The bursting defect in the inner tube is usually smaller than

the rent in the outer tube; it may retract beneath the edge of the outer tear. When there are multiple lacerations, complete rupture through all the layers is usually found in only a few, perhaps in only one of them. The most common lesion is a complete perforation at the angulation where the sigmoid colon joins the rectum, as in Case 3.

Figure 2 shows the approximate distribution of perforations in 32 cases. Autopsy records of some of the cases in Table I indicate that the injury destroyed the blood supply of segments of the colon (Buchbinder[7]); but this seems to be rare. Tearing of the ascending and descending colon from parietal attachments, as in Case 1, has been observed in a number of cases. The entire intestinal canal may be filled with air. It is difficult to understand how the air got into the gallbladder in Case 1. Subcutaneous emphysema of the trunk occurs when the distention is great.

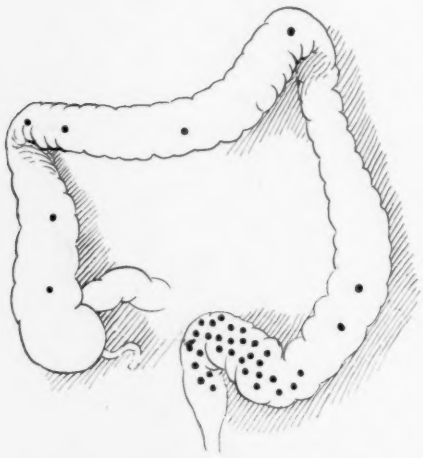

FIG. 2.—Schematic drawing showing the approximate location of 38 perforations in 32 cases. Two cases each, had three perforations in the sigmoid colon. One case had two perforations in the sigmoid colon. Twenty-nine cases had single perforations.

Mecray's case (Bendixen and Blything[6]), in which "the colon was ruptured in eight places," and others not definitely described as to location, are not included in the drawing.

Diagnosis.—The history in these cases has often been obscured by language difficulties, and by attempts to conceal the facts. There should be no difficulty in diagnosis from the history alone, when properly elicited. Abdominal pain is immediate, perhaps most severe in the upper part of the abdomen, radiating to the shoulders. The patient is usually prostrated. In the more severe cases, there is enormous ballooning of the abdomen, with cyanosis resulting from embarrassment of respiration and circulation. Subcutaneous emphysema of the trunk may be present. The uniformity of the tympany over the entire abdomen has been considered diagnostic.

When the distention is not great, the pain in the upper part of the abdomen may disappear, leaving the patient quite comfortable until local pain in the region of the perforation develops, as in Case 3. In this case, obliteration of the liver dulness was the only positive physical sign. Roentgenograms taken with the patient erect show the gas between the liver and diaphragm (Fig. 1).

Treatment.—When distention is great, immediate paracentesis should be performed. The general condition may improve remarkably after simple relief of intra-abdominal pressure; even moribund patients may rally sufficiently to warrant celiotomy. To illustrate the tension that may be present we will quote Wainwright (Ide[17]): "When the peritoneum was opened there was a loud escape of gas under high pressure, almost as loud as the report of a small automobile tire." Buchbinder's[7] description is also of interest in

this detail: "The transversalis fascia was not incised but sharp-nosed forceps were pushed through in order to control the escape of air. The fascia immediately tore like wet paper under great tension; the air rushed out with a report, and the abdominal wall dropped in. The sudden escape of air nearly proved fatal, but after a few moments the patient rallied, and his general condition seemed much improved."

Rectal tubes are of no avail. Enemata are of course very harmful. Ritchie's[18] case was given a soapsuds enema and then a turpentine enema at home before a doctor was called. The fluid was removed from the peritoneal cavity; the rent in the sigmoid was repaired—and the man recovered.

Operation should be performed as soon as possible. The incision should be large enough for exposure of all of the colon. The defects in the bowel should be closed as quickly as possible. Resection is of course necessary when the blood supply of the bowel has been destroyed by the injury. Usually, simple suture of the rent is sufficient, but it may be difficult because of the irregular shape of the bursting laceration, and because the tear in the mucosal layer does not correspond accurately to that of the muscular layers. Drainage is usually advisable, not only because of the contamination, but also because of doubt as to the adequacy of the closure of the bowel. Colostomy and enterostomy have been performed. If the perforation is at or near the sigmoid flexure, it is better to have a long soft rectal tube inserted while the abdomen is still open, and guide it past the site of injury. The postoperative care is that of any other potential peritonitis case.

Prognosis.—Many of the cases listed in the literature are of little value for statistics because insufficient information is given. Table III summarizes the results of treatment. Recovery is usual when only the serous and muscular coats are torn. However, most of the cases had one or more complete perforations; in this larger group the prognosis is grave unless an adequate operation is performed within a few hours.

TABLE III

RUPTURE OF COLON FROM COMPRESSED AIR

	Result Unknown	Recovered	Died	Mortality Percentage
Incomplete Rupture:				
(Operative cases only)				
Our case #2 and 4 cases from the literature		4	1	20%
Complete Perforation:				
Our cases #1 and #3 and 60 cases from the literature	1	19	42	69%
Treatment unknown			7	
Without operation		0	21	100%
With operation	1	19	14	42%

CONCLUSIONS

Pneumatic rupture of the colon is produced by a jet of compressed air, which readily passes through clothing and enters the anus. Perforation

occurs at the rectosigmoid angle or, less frequently, at some other flexure of the colon. Rarely, only the serous and muscular coats of the bowel are torn.

The diagnosis may be made on the basis of the history alone, or by the physical signs alone. Absence of liver dulness may be the only important early physical finding. Roentgenologic examination in the erect position, in order to demonstrate air between liver and diaphragm, is a valuable aid in doubtful cases.

When distention is great and respiration is embarrassed, paracentesis should be performed immediately. Early celiotomy with appropriate repair offers good hope of recovery.

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CONGENITAL MALFORMATIONS OF THE APPENDIX—A FAMILIAL DISEASE

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The frequent occurrence of appendicitis in members of the same family is known, and has been remarked by numerous authors.[1, 2, 3, 4, 5] Probably every physician knows, at first hand, of one or more families in which plural appendicectomies have been performed.

Baker,[6] and also Miss M. L. Nutt, submit several pedigree charts of families who have been subjected to many appendicectomies. Discussing this matter editorially, the Journal of Heredity states: "Genetic differences in resistance to bacterial infection, a peculiar configuration of the appendix, or other factors about which we at present know nothing, probably constitute a predisposition toward inflammation of the appendix. The result, when expressed in a pedigree chart, resembles what we get in the inheritance of a definite morphologic or physiologic difference, but the chain of events leading up to the 'expression' of the 'character' has at least one more link of crucial importance—an environmental trigger-stimulus of some kind."

If congenital anomalies of the appendix are truly a cause of symptoms and offer a predisposition to acute inflammation of the organ, this familial incidence is logical. Individual peculiarities of visceral organs ought to be as heritable as peculiarities of feature or complexion, or even of blood groupings, which have been shown by von Dungern and Hirschfeld[7] to be inherited.

Nicholson[8] has shown convincingly that mechanical deformities of the appendix are responsible for much ill health, poor nutrition and poor development in children. He also claims that many cases of appendicitis in later life can be traced back to childhood or infancy if a careful history is taken. The inference is that there is often a congenital fault. In my own experience, also, it had been common to find that the acutely inflamed appendix has been previously crippled by congenital bands or kinks, which may partially obstruct the lumen.

It seems of interest, therefore, to review the history of a family consisting of 22 individuals, representing one man and his descendants to the third generation, in whom appendicectomy has been performed in 16 instances. In every individual who has come to operation, the same deformity of the appendix has been found; and it seems likely that this deformity has been at least a predisposing cause of the disease.

The family studied includes N♂ 1, his six children and fifteen grandchildren. N♂ 1, four of the six children, and eleven of the fifteen grandchildren have been operated upon.

Individuals are distinguished in this study by their initials, the conventional sex symbol, and a numeral to distinguish whether they belong to the first, second or third generation; these symbols are used in the attached chart.

N ♂ 1, as far as known, had a healthy childhood and youth. No particular illnesses are remembered; on the contrary, he was strong and robust. All his immediate family had lived to a ripe old age, several surpassing 90 years. His sister, his brother, and his brother's four children have likewise had no appendiceal troubles; neither has there been any such in his wife or her family. The congenital mechanical fault that is found in so many of N ♂ 1's immediate descendants, and apparently inherited, seems to have been present in N ♂ 1 himself.

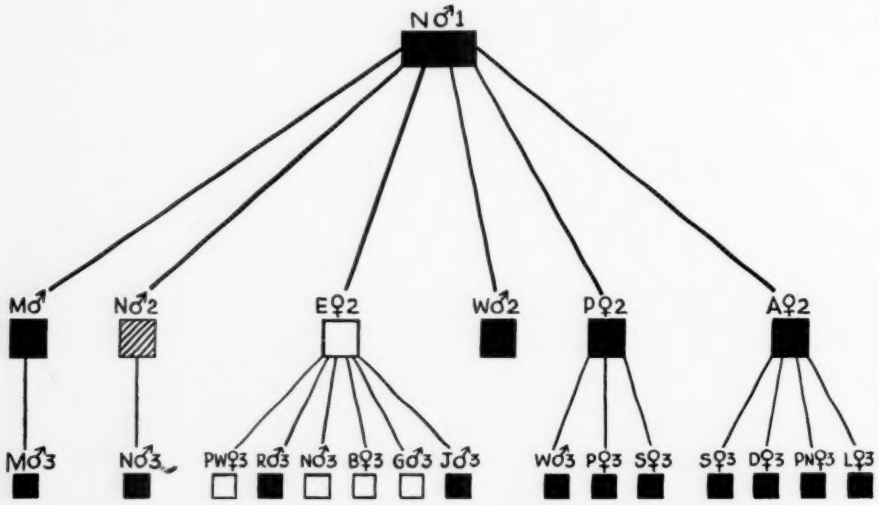

CHART 1.—The family tree of N♂ 1, showing frequency of occurrence of appendicitis in three generations. Key: Black—Operated for appendicitis. White—No symptoms of appendicitis, never operated upon. Shaded—Symptoms of appendicitis, but no operation.

This man, a physician, began around the age of 35 to have mild attacks that he diagnosed himself as appendicitis. But, in 1906, appendicectomy was not usually undertaken lightly, so for some years nothing was done. Finally, when he was about age 45, he was operated upon. His appendix was sharply kinked at the base by a band of fibrous tissue, which bound it to the outer side of the cecum—this is the deformity that has been found in every one of his children and grandchildren who have been operated upon. The operation was followed by complete relief of symptoms and freedom from the attacks of abdominal pain and vomiting, until his accidental death a few years later.

Though N ♂ 1 was the oldest of the family, he was not the first to require operation. Already, some years earlier, his fourth child, W ♂ 2, had been hurried to the hospital, and operated upon for acute appendicitis. The records of this illness were very poorly kept; but the boy ran a high temperature for ten days, and was in the hospital three weeks, leaving for home by ambulance. He finally made a perfect recovery.

No more surgery was necessary in the family for ten years or so. During this time N ♂ 2 often confided to his brother, a medical student, that he had a good deal of indigestion, with pain in his abdomen, from time to time, when a point of tenderness could usually be found at McBurney's point. However, the medical student rather feared ridicule if he "stuck his neck out too far," and dared not make the diagnosis of subacute appendicitis, which now seems obvious. Nothing was done. He was admitted into the Air Service in the first World War, serving under the command of Major Fiorello La Guardia, and was killed at the front, with his appendix still *in situ naturalis.*

After the war, the next beneficiary of surgery was M ♂ 2, who, a physician like his father, also made his own diagnosis. This was an acute attack of appendicitis, and had not been preceded by any prodromal symptoms. However, the appendix was acutely inflamed, and there was a similar congenital band and kink such as had previously been found in both his father and brother.

The two sisters P ♀ 2 and A ♀ 2 were next. P ♀ 2 was emaciated, constantly suffered with indigestion, and had McBurney's point tenderness. She was operated upon, and a kinked, deformed appendix was removed, which was not acutely inflamed, but was found in the usual familial position. A ♀ 2 was more robust, but had had many sharp attacks of so-called "colic." From her was removed an acutely inflamed appendix. Both these women have been entirely free of indigestion and colic ever since.

E ♀ 2 has never had any troubles with her own appendix, and only two of her six children have been operated upon as yet. The two boys R ♂ 3 and J ♂ 3 both had acute attacks of appendicitis, and showed the familial deformity seen in all the other cases.

M ♂ 3 was the son and grandson of physicians; so when he began to have indigestion and abdominal pains at the age of eight, no time was lost waiting for a second attack. His appendix promptly came out. It was not acutely diseased, but was deformed.

N ♂ 3 was the only child of a widow, who was not thoroughly convinced that promiscuous appendicectomy was a good thing. So he continued to be allowed to suffer from indigestion and abdominal pains till the age of 19. At this time, his appendix gave real trouble, for at operation, about eight hours after the onset of an attack, it was found to be already ruptured. He made a good recovery, and has since been entirely free from discomfort.

The next three grandchildren consist of the son and two daughters of P ♀ 2. Their father and mother have both been appendicectomised. These three children all had mild or severe, acute attacks in early childhood; P ♀ 3, the oldest daughter, drained for several weeks. All had the usual deformity and constriction of the lumen of the appendix; and all have been perfectly well since their operations.

The four daughters of A ♀ 2 have also all been operated upon, with the same operative findings; and the same improvement in health as in the patients noted. Three had acute attacks; one, S ♀ 3 had a chronic condition, with so much anorexia, pylorospasm, and vomiting, that she nearly died of starvation. She was operated upon in 1927, at the age of four, when it was not realized that appendiceal deformities could cause such a serious situation. Her operation was undertaken with a great deal of hesitation by all concerned. The child's almost instant recovery, with gain in weight and strength, was one of the most dramatic things I have ever seen.

Most of the patients mentioned have, by now, reached adult life, though two are still children. All are now normal, healthy individuals, entirely free of any digestive or abdominal disturbances.

It is astonishing, in reading the histories of these cases, to note the close familial resemblance of all these appendices. Though the operations were performed in various hospitals, and the findings recorded by various interns between 1909 and 1938, in every case the record refers to a band of fibrous tissue at the base of the appendix, with more or less adhesion of the organ to the outer surface of the cecum, exactly as in the case of N ♂ 1, the founder of the family.

This family history emphasizes the remarks made as long ago as 1886 by Reginald Fitz,[9] who stated that: "In considering the symptoms of appendicitis, it is to be noted that attacks of inflammation frequently occur without giving rise to any characteristic symptoms, and often without suggestion of any distinct malady . . . The severity (of the lesions found at autopsy) suggests the

probability that apparently slight disturbances of digestion were overlooked. The diarrhea, constipation, or abdominal pain, especially when occasionally recurrent, were regarded as characteristic of a feeble digestion. There can be little doubt that a diagnosis of bilious attack, colic, gastritis, enteritis, gravel . . . and the like, may not infrequently conceal the existence of an inflamed appendix." Most of these diagnoses have been made in the histories of the second generation of this family. Truly it is said—"There is no new thing under the sun."

SUMMARY AND CONCLUSIONS

This is the history of a family consisting of 22 members—being one man, his six children and fifteen grandchildren, in whom appendicectomy has been performed in 16 instances.

Most of the operations were performed during early childhood. In the adults, most of the symptoms mentioned by Nicholson can be traced back to childhood in nearly all of the cases.

The strikingly good results which, as he shows, follow removal of the mechanically crippled appendix, are borne out in this family.

It is believed that these crippling peritoneal bands may be inherited.

Most of the specimens removed were considered merely routine appendices, and were not particularly examined by the several pathologists. It is believed that the earliest symptoms are due to deranged intestinal function only, of a reflex nature, such as pylorospasm or spastic colon, without organic changes in the appendiceal wall. This was certainly true of S♀ 3; but this series throws little light on this question, which I hope to consider at another time.

The presence of congenital malformations alone is not sufficient to precipitate an attack of acute appendicitis, though they are a predisposing cause. To produce the acute attack, the presence of some other etiologic factor is necessary.

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OBSTRUCTIVE JAUNDICE DUE TO CARCINOMA OF THE PANCREAS: THE CHOICE OF OPERATIVE PROCEDURE

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DESPITE recent renewal of interest in the problem of biliary tract obstruction due to carcinoma of the head of the pancreas, treatment of this condition remains as yet almost entirely palliative in nature.

Whipple, and his associates[15, 18, 19] have made encouraging progress with their operation for neoplasm arising from the ampulla of Vater. However, the multiple-stage procedure which they advocate has been marked, even with them, by a rather high mortality rate. As far as published reports show, they have apparently had two successful resections for carcinoma of the ampullary region.

Clinical instances of radical resection of the head of the pancreas for carcinoma, attendant with any degree of success, are extremely few. The patient reported by Brunschwig[1] succumbed to local recurrence and hepatic metastases before leaving the hospital. Recently, a case of successful resection was reported by George Crile, Jr.,[4, 5] and another has been added by Illingworth.[9] Otherwise no claims of pancreatic head excision with recovery have been published to our knowledge.

Formidable anatomic barriers, chiefly the intimate fixation of the portal and the superior mesenteric vein to the pancreas, seem to preclude the likelihood of further technical advances in this field. In Brunschwig's case, resection appears to have been facilitated by the existence of an unusually mobile pancreas, a favorable circumstance which can rarely be found in the human subject. The operative descriptions of Crile and Illingworth would suggest that the amount of pancreatic tissue resected by each was small.

Thus, for the present at least, the surgeon must be content with measures which afford only symptomatic benefit to patients with carcinoma involving the head of the pancreas, and in most cases of ampullary malignancy as well. Essentially his efforts must be restricted to the relief of the resultant mechanical interference with excretion of bile and the accompanying severe organic changes and subjective manifestations of complete obstructive jaundice.

These patients, as a rule, are poor subjects for an extensive surgical procedure. They are usually at or beyond middle age. They are debilitated. They are enfeebled by the effects of progressive and profound cholemia, with its related physiochemical disturbances. They are liable to hemorrhage. They suffer from biliary infection, to a greater or lesser degree. The situation is analogous to intestinal or urinary tract obstruction. The immediate need is for relief of the obstruction. The procedure to be adopted should be one which effectively fulfills this purpose, with minimum risk.

Two types of palliative operations are available in dealing with carcinoma of the head of the pancreas. The choice of procedure lies between reestablishing bile flow into the intestinal tract by anastomosis or by providing biliary excretion through external drainage. Of these two measures, the former has been almost routinely adopted by most surgeons when palliation has been sought.

It has been our impression for some time that biliary-intestinal anastomosis, as a primary procedure, is rarely warranted in these cases. This opinion has been formed through personal experiences and from critical review of the published results of other observers. The high immediate operative mortality rate associated with internal drainage of the biliary tract does not appear to justify its routine employment.

For these reasons, during the last two years (1938 and 1939), it has been our practice to provide only gallbladder or common duct drainage as the initial surgical step in most cases of complete obstructive jaundice due to chronic pancreatic disease. The purpose of this communication is to review this subject in the light of our experience and particularly to compare the results obtained with external drainage as opposed to internal biliary decompression. These two methods will be judged chiefly with regard to operative mortality, symptomatic relief, and length of postoperative survival.

Published statistics dealing with mortality rates in palliative operations for carcinoma of the head of the pancreas are not encouraging. They deal chiefly with the procedure of primary biliary-intestinal anastomosis. The immediate mortality rate averages between 30 and 50 per cent. Hunt and Budd[8] state that the mortality in anastomotic operations "approaches 70 per cent." Judd and Parker[10] had 18 deaths in 34 cases of anastomosis in pancreatic carcinoma. Fraser's[7] mortality rate, in a large compiled series, with primary cholecystogastrostomy, for malignant cases, was 51.8 per cent. Oppenheimer, Glass, and Netter[12] found a mortality rate of 44.1 per cent, with primary internal drainage. Eliason and Johnson[6] had an operative mortality of 40 per cent, with cholecysto-enterostomy. Somewhat lower are the figures of Cohen and Colp,[2] 32 per cent; Zollinger and Kevorkian,[19] 31 per cent; and Ransom,[15] 29.17 per cent. The former found a greater mortality with simple abdominal exploration alone, than with anastomosis, which would suggest that sidetracking of the biliary flow was reserved for the less desperate cases. The lowest reported mortality is that of Coller and Winfield,[3] 26 per cent, but their series included a large proportion of cases in which the biliary obstruction was due to stone and other benign lesions.

The only available data comparing the operative mortality rates of external with internal drainage of bile for obstructive jaundice due to chronic pancreatic disease is that given by Fraser,[7] who found an operative mortality rate of only 11.6 per cent in 84 cases of surface drainage, and 24 per cent in anastomosis performed after initial biliary decompression. In the same collected series, the immediate operative mortality rate with primary cholecystogastrostomy for pancreatic malignancy was 51.8 per cent. The contrast is striking

and merits consideration. Walters,[16] some years ago, also called attention to the advisability of delayed anastomosis but gave no data in his paper.

A striking uniformity is found in the postoperative survival period of these cases as reported by various authors. Palliative procedures, while materially adding to the comfort of patients with carcinoma of the head of the pancreas, have little effect in prolonging life expectancy. Most patients succumb within six months after operation; few are alive after one year. The average duration of life postoperatively, even allowing for rare instances of unusually long survival, is between seven and eight months. Fraser, in his series, found 66 per cent dead under six months, and 90 per cent within 12 months. The average survival periods reported by other authors are as follows: Zollinger and Kevorkian, 9 months; Judd, 7.3 months; Lahey,[11] 8.6 months; Coller and Winfield, 7.2 months; Eliason and Johnson, "short"; Oppenheimer, Glass, and Netter, 7 months. Oppenheimer[13] reported one unusual instance of long postoperative survival (29 months).

Findings.—During the ten-year period (1930–1939 inclusive), 106 patients were operated upon on the Surgical Ward Services of the Mt. Sinai Hospital, with the diagnosis of carcinoma of the head of the pancreas. The mortality rate for the entire series was 33 per cent (35 operative deaths in 106 cases). Biliary-intestinal anastomoses were performed in 50 of these patients, with 24 deaths, an operative mortality rate of 48 per cent. In contrast to these high figures, 27 patients had external biliary drainage, alone, as the primary operative procedure, with three deaths, a mortality rate of only 11.1 per cent. In the remaining 29 cases of this series, operation was limited to abdominal exploration. In this group, there were eight deaths with a mortality rate of 27.5 per cent. These findings are tabulated in Table I:

TABLE I

	No. of Cases	No. Died	Mortality %
Total	106	35	33
Anastomosis	50	24	48
External drainage	27	3	11.1
Celiotomy only	29	8	27.5

In the latter two years of this study, primary anastomoses were reserved for the younger, incompletely-obstructed and better risk cases. For the others, a careful routine of preoperative preparation, minimal operative manipulation, and subsequent care was followed. Operation was withheld for several days to permit administration of fluids and improvement of liver function. Most patients received one or more transfusions of fresh citrated blood. All were given bile salts and vitamin K orally.

The operations were performed under local novocain anesthesia, through a short subcostal incision. Exploration was limited to steps essential for confirmation of the diagnosis of noncalculous obstruction. When the gallbladder was found distended, and the pancreatic head enlarged, by digital examination, cholecystostomy was performed without exposure of the pancreas and without attempting to obtain a biopsy specimen. The common duct was drained

by T-tube in those patients where the gallbladder was absent due to previous operation.

Two or three weeks after operation, visualization of the biliary tract was obtained by roentgenographic study following injection of lipiodol through the cholecystostomy tube. This was done to guard against the possibility of overlooking common duct or ampullary stones and to reveal the site and degree of obstruction due to extrinsic pressure.

The patients were discharged from the hospital with the drainage tube left indwelling. Bile salt therapy was continued. They were seen periodically for follow-up examinations. In the instances where good general condition was maintained after four months, lipiodol studies were repeated. When complete common duct obstruction persisted, though the patient remained well and continued to gain weight and strength more than six months after operation, it was assumed that the diagnosis of pancreatic malignancy was probably incorrect. These patients were returned to the hospital for further study and reoperation. They were now in far better condition for abdominal exploration, and possible anastomosis, than at the time of the original drainage.

During this period of study, operation was performed upon 28 patients with obstructive jaundice due to chronic pancreatic disease. There were five deaths, giving a total mortality rate of 17.8 per cent. Cholecystostomy or choledochostomy, or both, were carried out in 16 of these cases with two deaths (12.5 per cent). There were three deaths in eight instances of biliary-intestinal anastomosis, a mortality rate of 38.5 per cent. Four patients had celiotomy only. The contrast with the preceding period, in which primary anastomosis was performed in a majority of the cases, is demonstrated in Table II.

TABLE II

1930–1937	No. of Cases	No. Died	Mortality %
Total	78	30	38.4
Anastomosis	42	21	50
External drainage	11	1	9.1
Celiotomy only	25	8	32
1938 and 1939	**No. of Cases**	**No. Died**	**Mortality %**
Total	28	5	17.8
Anastomosis	8	3	35.8
External drainage	16	2	12.5
Celiotomy only	4	0	0

Late follow-up records were available in 62 of the 71 patients who survived and left the hospital after operation. Only nine are known to be alive at the present time, the remaining 53 having succumbed to carcinoma at varying times, usually within a few months postoperatively. These findings are shown in Table III.

The life expectancy of these patients is brief. Over 80 per cent are dead within one year after operation. The average survival period is only 5.5 months. It is not materially influenced by the type of palliative procedure em-

ployed. The few instances of prolonged survival may generally be regarded as nonmalignant cases.

Analysis of Findings.—It is evident that anastomosis between the biliary and intestinal tracts in the presence of complete obstructive jaundice is an undertaking of great hazard. It invites an operative mortality rate of nearly 50 per cent. This in contrast with a mortality rate of only 10 to 12 per cent for external biliary drainage. The benefit to the patient as regards relief of discomfort and length of postoperative survival period is about the same with either procedure. The disparity between the relative risk of internal as opposed to external drainage is striking (5:1).

A case report is given to illustrate the advantage of delayed anastomosis.

TABLE III

LENGTH OF POSTOPERATIVE SURVIVAL

	Biliary-Entero-anastomosis	External Drainage	Exploratory Celiotomy	Total
No. Followed	25	18	19	62
Died:				
Under 6 mos.	16 (64%)	7 (38.8%)	12 (63.2%)	53 (85.5%)
6–12 mos.	6 (24%)	4 (22%)	5 (26.3%)	
1–2 yrs.	1 (4%)	1 (5.5%)		
Over 2 yrs.	1 (4%)			
Average survival period	6.3 mos.	6.1 mos.	5.1 mos.	5.5 mos.
Alive	1 at 1 yr.	4 over 1.5 yrs.	1 over 5 yrs.	
				9 (14.5%)
		2 at 8 mos.	1 at 3.5 yrs.	

Case Report.—Hosp. No. 435647: J. S., male, age 51, was admitted to the hospital, February 1, 1939, having been ill for seven weeks with mild, upper abdominal discomfort, progressively increasing jaundice, and the loss of 17 pounds in weight. He appeared much older than his age; feeble and deeply icteric. A globular mass was palpable beneath the liver edge. His stools were clay-colored. The urine contained much bile, and only a trace of urobilin. Blood cholesterol was 400 mg. per cent; cholesterol 280, and the icterus index 38.

This patient presented a grave risk for primary cholecystogastrostomy. Cholecystostomy was performed with minimal exploration. He gained rapidly postoperatively. His jaundice cleared promptly. He was discharged six weeks after the first operation, with a biliary fistula and followed as an out-patient.

Eight months later his condition was excellent, despite persistence of complete common duct obstruction. It was felt that he might have chronic pancreatitis rather than carcinoma. He was readmitted to the hospital, and secondary cholecystogastrostomy was performed, October 15, 1939. Convalescence was uneventful. When seen over one year after his initial operation, he was symptom-free and had regained his maximum weight. His operative wound was healed, his stools were brown, and his general condition good.

COMMENT.—Attempts to restore continuity of bile flow into the intestinal tract by anastomosis with the gallbladder or common duct, in the presence of obstructive jaundice due to carcinoma of the pancreas have resulted, consistently, in a high percentage of operative deaths. Of those who survive operation, the average life expectancy is only a few months.

Reestablishment of bile flow into the intestinal tract is of little practical importance. It does not lengthen the survival period nor add materially to the comfort of the survivor beyond results obtained by the surface drainage

of bile. The oral administration of bile salts and vitamin K adequately compensates for lack of bile in the bowel. Palliation can be as effectively accomplished in these cases by the relatively simpler and less hazardous procedure of creating an external biliary fistula through cholecystostomy or choledochostomy.

SUMMARY AND CONCLUSIONS

(1) Radical excision of carcinoma involving the head of the pancreas is rarely possible.

(2) The choice of palliative procedure lies between biliary-intestinal anastomosis and external biliary drainage.

(3) In our series, primary anastomosis resulted in an operative mortality rate of 48 per cent (24 deaths in 50 cases).

(4) Contrasted with this high figure was a mortality rate of 11.1 per cent when the initial operation was restricted to external drainage alone (27 cases with three deaths).

(5) Symptomatic improvement and the postoperative survival period in the externally drained cases was as good as with anastomosis.

(6) An operative procedure which carries a mortality risk of almost 50 per cent does not seem warranted when the survivors can expect to live only a few months after operation.

(7) Since chronic pancreatitis cannot, with certainty, be differentiated from carcinoma even at operation, those patients who might otherwise survive if simple biliary decompression were instituted are sometimes subjected needlessly to the same risk as cancer patients.

(8) It is recommended that, except in the rare cases of young patients in good general condition, noncalculous, complete obstructive jaundice be treated surgically by simple decompressive operation alone, as the initial operative procedure.

(9) Those patients who are alive and in good condition more than six months after operation may be assumed to have benign rather than malignant lesions of the pancreas.

(10) If common duct obstruction persists, they can then be operated upon again with relative safety, and the continuity of bile flow into the intestinal tract restored.

(11) This procedure has been followed on our service at the Mount Sinai Hospital during the last two years with encouraging results.

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ILEUS FOLLOWING FRACTURED RIBS

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FRACTURE OF RIBS complicated by paralytic ileus is rare. We have been able to find only five cases reported to date. Adams[1] described the first two in 1910, Ralphs[2] cited the third in 1925, and Vandel[3] reported the fourth in 1926. Christopher,[4] in 1929, summarized the previously reported four cases and added the fifth.

The rarity and severity of this complication when it does occur, make this condition interesting and worthy of study. Among the 454 cases of fractured ribs seen at the Henry Ford Hospital during the past 24 years, there have occurred 10 cases of paralytic ileus complicating the injury. Only cases of fractured ribs uncomplicated by conditions such as pneumonia, fractured pelvis, or fractured vertebrae, which are known to produce ileus, are included in this study. Brief reports of these cases follow:

CASE REPORTS

Case 1.—J. T., white, male, age 31, while riding a motorcycle, collided with a car December 2, 1926. He was brought to the Henry Ford Hospital immediately. Roentgenologic examination showed fractures of ribs 8, 9 and 12 on the left side, 5 cm. from the lateral margin of the vertebral column. There were no abdominal symptoms. Leukocytes 15,200, with 79% polymorphonuclear cells. On December 5, 1926, marked abdominal distention developed and persisted for two days, being treated conservatively with hot water bottles to the abdomen, enemata and cathartics. The distention gradually disappeared, and his course was uneventful. He was discharged December 14, 1926.

Case 2.—D. D., white, female, age 54, tripped and fell across a bucket February 6, 1933, striking her left chest. She was taken immediately to the Henry Ford Hospital and roentgenologic examination revealed fractures of ribs 10, 11 and 12 on the left side, 10 cm. from the lateral vertebral border. There were no signs or symptoms pointing to any intra-abdominal injury. Marked distention developed which was treated with enemata and insertion of a rectal tube. It subsided completely in 36 hours.

Case 3.—T. C., white, male, age 32, was struck by an automobile May 12, 1935, and was admitted to another hospital. On May 14, 1935, he was transferred to the Henry Ford Hospital where roentgenologic examination showed fractures of ribs 3 and 4 on the right side, near their articulations with the spine, and fractures of ribs 5, 6 and 8 on the right side, at the posterior axillary line. There was also a fracture of the left humerus. On the day following admission abdominal distention associated with repeated vomiting developed. On May 16, 1935, the distention continued with the patient vomiting small amounts frequently. Gastric aspiration and lavage, repeated enemata, and multiple doses of pitressin and prostigmin were necessary to control the distention, which finally subsided on May 17, 1935. Convalescence was slow and he was discharged June 13, 1935.

Case 4.—C. T., white, male, age 24, was injured in an automobile accident October 13, 1935. He was admitted to the Henry Ford Hospital on October 16, 1935, because of

pain in the left chest. There were no signs of any intra-abdominal injury. Leukocytes 10,100, with 84% polymorphonuclear cells. Roentgenologic examination revealed fractures of ribs 7, 8 and 9 on the left side, 1.5 cm. from the lateral vertebral border, and fracture of the tenth left rib, 5 cm. from the vertebral border. Moderate abdominal distention was noted October 18, 1935, which was treated conservatively, subsiding 24 hours later. Convalescence was slow because of the development of a traumatic pleurisy, and he was discharged November 25, 1935.

Case 5.—J. Van H., white, male, age 55, was admitted to the Henry Ford Hospital December 17, 1936, because of abdominal distention, vomiting and constipation of 24 hours' duration. On December 15, 1936, he had fallen eight feet from a ladder, striking his chest on the back of a sofa. His physician had made a diagnosis of fractured ribs and had strapped his chest. Roentgenologic examination revealed fracture of the fourth rib on the left side, 2 cm. from the vertebral border, and, also, fracture of the eleventh rib on the left side, 7.5 cm. from the vertebral border. Treatment with numerous enemata and repeated doses of pitressin was effective. The abdominal distention subsided 3½ days after admission, and he was discharged December 22, 1936.

Case 6.—W. D., white, male, age 41, was injured in an automobile accident January 3, 1938. He was given emergency treatment at a hospital in the vicinity, and was then transferred to Henry Ford Hospital. Roentgenologic examination showed fractures of ribs 3, 4, 5, 6, 7, 8, 9, 10 and 11 on the left side. The third rib was fractured in the axillary line, while the remainder were fractured 2.5 cm. or less from the vertebral borders. The eighth and ninth ribs were also fractured in the posterior axillary line, and there was a comminuted fracture of the clavicle. Abdominal distention developed January 5, 1938, and was of marked severity the following day, but disappeared January 7, 1938. Treatment consisted of gastric aspirations, frequent enemata, and repeated doses of pitressin and prostigmin. His course was further complicated by the development of a saphenous phlebitis. He was discharged February 25, 1938.

Case 7.—E. M., white, male, age 45, fell 15 feet, striking his left chest May 17, 1938. He was admitted directly to the Henry Ford Hospital in shock. Roentgenologic examination revealed fracture of the ninth rib 5 cm. to the right of the vertebral column, of the tenth right rib, which was markedly comminuted near its articulation, and of the eleventh right rib 5 cm. from the vertebral border, with marked comminution. The seventh and ninth ribs on the right side were fractured in the anterior axillary line. A tension pneumothorax developed, and was treated with an intercostal tube leading to a water-seal. Abdominal distention appeared 48 hours after the accident and persisted for two days, gradually subsiding under treatment with frequent enemata and repeated injections of pitressin and prostigmin. He was discharged June 17, 1938.

Case 8.—A. J., white, male, age 58, was admitted to the Henry Ford Hospital May 19, 1939, after he had slipped and struck his right chest when getting out of the bath tub. Roentgenologic examination showed fracture of ribs 6, 7 and 8 on the right side, in the midaxillary line, and fractures of the tenth and eleventh, 3 cm. to the right of the vertebral border. Abdominal distention developed May 21, 1939, and he was treated with enemata; subsiding in 24 hours. He was discharged May 22, 1939.

Case 9.—G. B., white, male, age 40, was injured in an automobile accident November 2, 1939, and 11 hours later he was admitted to the Henry Ford Hospital. The abdomen was moderately distended on admission. Roentgenologic examination showed fracture of the third rib on the right side, in the midaxillary line, and fractures of ribs 3, 4, 5 and 6 on the left side, in the midaxillary line. Abdominal distention persisted from the time of admission until November 6, 1939. Treatment consisted of repeated enemata, injections of pitressin, and the introduction of a rectal tube. Continuous oxygen was administered from November 2, to November 12, 1939. He was discharged November 23, 1939.

Case 10.—J. M., white, male, age 48, was injured March 28, 1940, when his chest was caught between a steel box and a door-jack. He was unconscious for a short period following the accident. Roentgenologic examination revealed fractures of ribs 5, 6 and 7

on the right side, in the midaxillary line, and a second fracture of the sixth rib, 2 cm. to the right of the vertebral border. Abdominal distention appeared 24 hours after the accident, and persisted for two days. Numerous enemata, and repeated injections of pitressin and prostigmin effectively controlled the distention. A flat film of the abdomen showed dilated loops of small and large intestine. The patient was discharged April 6, 1940.

TABLE I

DISTANCE OF FRACTURE SITE FROM VERTEBRAL MARGIN AS SEEN ROENTGENOLOGICALLY

Case	Sex	Ribs Fractured	Side	Distance from Vertebral Margin
1. (86697)	M.	8, 9 and 12	L.	5 cm.
2. (6763)	F.	10, 11 and 12	L.	10 cm.
3. (212352)	M.	3, 4, 5, 6 and 8	R.	3–4 cm.
4. (224589)	M.	7, 8 and 9	L.	1.5 cm.
		10	L.	5 cm.
5. (58476)	M	2	L.	2 cm.
		11	L.	7.5 cm.
6. (268379)	M.	2	L.	11 cm.
		4, 5, 6, 7, 8, 9, 10	L.	2.5 cm.
		8 and 9	L.	11.5 cm.
		11	L.	0.5 cm. (comminuted)
7. (275227)	M.	7 and 8	R.	Anterior axillary line
		9 and 11	R.	5 cm.
		10	R.	0.5 cm. (comminuted)
8. (292902)	M.	6, 7 and 8	R.	Midaxillary line
		10 and 11	R.	3 cm.
9. (184866)	M.	2	R.	Midaxillary line
		3, 4, 5 and 6	L.	Midaxillary line
10. (309371)	M.	6	R.	2 cm.
		5, 6 and 7	R.	Midaxillary line

NOTE: Since it is impossible to measure accurately the fracture site beyond the axillary line on the roentgenogram, measurements beyond this point are not given.

An analysis of these cases (Table I) shows that eight out of ten (80 per cent) had one or more fractured ribs within 5 cm. of the lateral vertebral border. In two instances the head of the rib was badly comminuted. It is notable that all of these cases, except one, were males. The five previously reported cases were also males. The ages varied from 24 to 58 years, the average being 46.8.

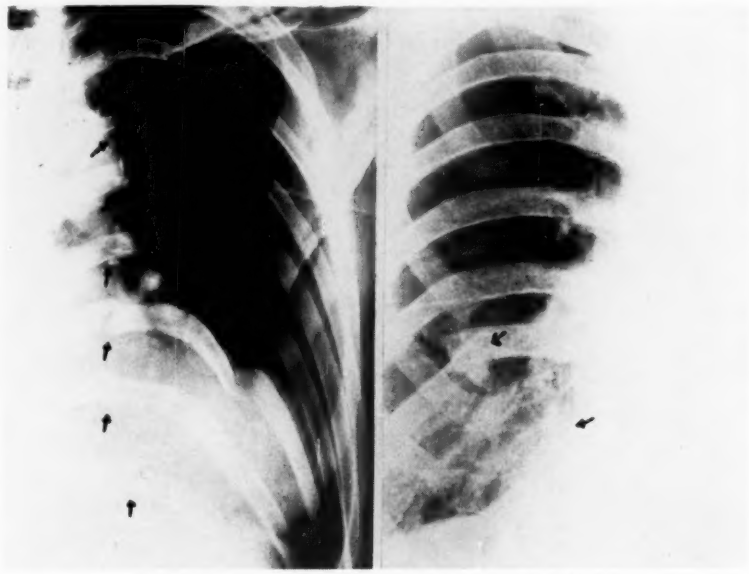
The abdominal distention appeared ten to 8.4 hours after the injury (Table II).

TABLE II

THE TIME OF ONSET OF THE ILEUS IN THE PRESENT SERIES OF TEN CASES

Number of Cases	Time of Onset (Hours)
2	10–12
3	13–24
1	25–48
3	49–72
1	73–84

The ileus that occurred was paralytic in type, and varied in severity. The distention lasted from one to six days, and in eight cases the duration was two or more days. As soon as the distention was noted, energetic treatment for its control was promptly started. This usually consisted of close observation, repeated enemata, use of the rectal tube, and doses of pitressin or prostigmin at intervals of one or two hours. In three cases gastric aspirations and lavage were necessary.



Case No. 6. Case No. 7.

FIG. 1.—Reproductions of roentgenograms illustrative of paravertebral fractures.

Although five of the cases had a prolonged convalescence and period of hospitalization greater than 25 days, all of the patients recovered under this treatment without operation. We believe that if the presence of a ruptured intra-abdominal viscus can be ruled out, as it was in these ten cases, this type of patient is best treated conservatively without operation. The difficulty arises in the differential diagnosis between this type of reflex paralytic ileus and distention secondary to intra-abdominal injury. The upper abdominal muscle spasm secondary to irritation of the lower intercostal nerves by the fracture adds to this difficulty.

Discussion.—In Figure 2, it is seen that the thoracic portion of the ganglionated sympathetic cord is situated on the heads of the ribs beneath the parietal pleura and just lateral to the bodies of the thoracic vertebrae. The three splanchnic nerves arise from the lower portion of the thoracic cord and are distributed to structures in the abdominal cavity. The great splanchnic nerve[5] arises by a series of roots from the fifth to the ninth ganglia inclusive. The small splanchnic arises from the ninth and tenth, or tenth and eleventh

ganglia or from adjacent portions of interganglionic cords. The least splanchnic arises from the lowest of the thoracic ganglia and may receive a filament from the small splanchnic, from which it occasionally takes origin. Rarely, a fourth splanchnic nerve is formed by filaments from the cardiac nerves aided by twigs from the lower cervical and upper thoracic ganglia. The efferent splanchnic fibers, after passing through the ganglionated cord, are distributed below the diaphragm as viscero-inhibitory fibers to the stomach and intestine, motor fibers for a portion of the circular muscle of rectum,

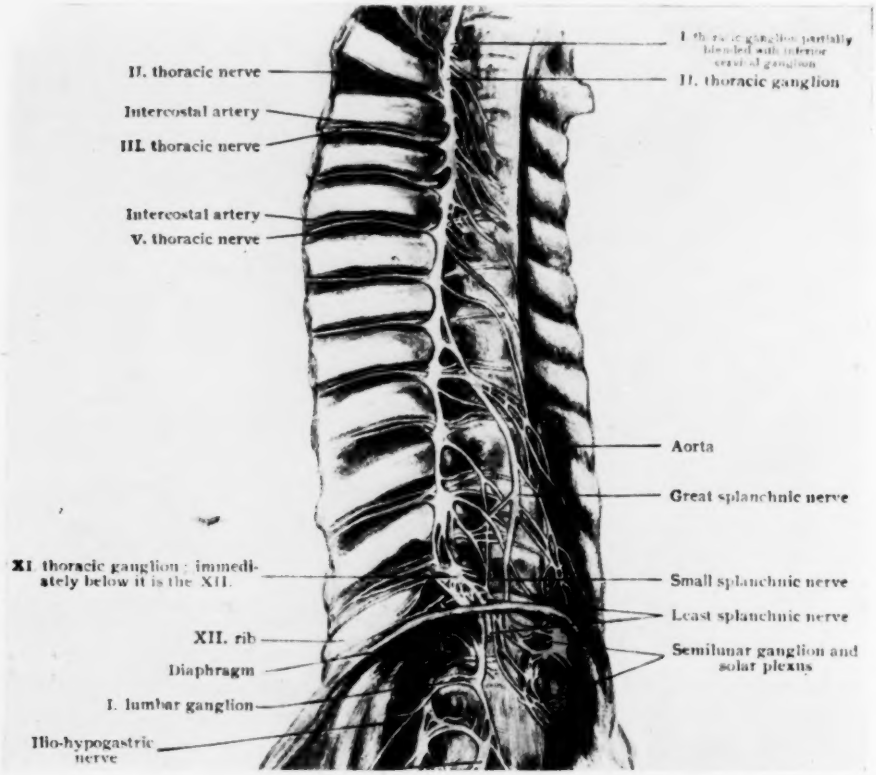


FIG. 2.—Showing the thoracic portion of the ganglionated sympathetic cord and the splanchnic nerves. (Human Anatomy, Piersol., J. B. Lippincott Co., Philadelphia, 5th Edition, 1916).

vasomotor fibers for the abdominal aorta and its branches, and secretory and sensory fibers for the abdominal viscera. The vagus and splanchnic nerves act as antagonists to each other, the vagus being motor and the splanchnics inhibitory in action. Division of the splanchnics causes marked increase in the intestinal movements, while stimulation of the splanchnics causes a cessation of movements and relaxation of the small bowel (Bayliss and Starling,[6] Macleod[7]). Chemical or electric stimulation of the splanchnics leads to distention and paresis of the entire small intestine.[8] It is evident then that the sympathetic ganglia, resting on the heads of the corresponding ribs, give rise to the splanchnic nerves which supply inhibitory fibers to the stomach and

intestine. Artificial stimulation of the splanchnic nerve produces relaxation and cessation of movement of the small bowel.

The mechanism by which paralytic ileus is produced by fracture of one or more ribs is not clearly understood. Adams[1] believed that some displacement of the proximal portion of the fractured rib occurs, producing irritation of the sympathetic chain of the thoracic ganglia and the splanchnic nerves arising from them. Vandel[3] believed that, anatomically, it was difficult to understand how the proximal rib fragment, which is strongly bound to the vertebral column by ligaments, could move to the extent necessary for this explanation to apply, although the point of fracture in his case was one inch to the right of the vertebral border. Morton[8] states that the traumatic effects are supposed to be reflex through the peripheral nerves to the sympathetic ganglia stimulating the sympathetics. Eight out of our ten had one or more rib fractures within 5 cm. of the lateral vertebral border, and in two instances the actual head of the rib was comminuted. From a study of these cases we believe there are four possible means of splanchnic stimulation:

(1) Irritation of the sympathetic thoracic ganglia and, therefore, the splanchnic nerve may occur through some displacement of the proximal rib fracture segment as first suggested by Adams.[1] At least in those cases in which the head of the rib was comminuted, it is evident that sufficient displacement could occur.

(2) Edema of the tissues adjacent to the point of fracture may encroach upon the position of the thoracic sympathetic ganglia.

(3) Retropleural hematoma in the vicinity of the thoracic sympathetic ganglia or splanchnic nerves resultant from the trauma may produce pressure on the sympathetic ganglia and splanchnic nerves. Demel[9] has shown that an experimentally produced hematoma in the region of the splanchnic nerve causes a paresis and a meteorism of the entire small bowel.

(4) Stimulation of the peripheral nerves either intercostal or abdominal may result in reflex stimulation of the splanchnics through the thoracic ganglia, as suggested by Ralphs.[2] This, possibly, would explain the development of ileus after rib fracture located some distance from the spine. Olivecrona[10] noted that strong sensory stimuli, such as crushing of the testes, produce a powerful inhibition of peristalsis by reflex stimulation of the splanchnics. If the splanchnics are divided, this reflex inhibition of peristalsis will not occur. Another example of dilatation of the stomach and small intestine caused by reflex stimulation of the splanchnics is seen in the abdominal distention occasionally seen with renal colic (Eisendrath[11]).

SUMMARY AND CONCLUSIONS

(1) Intestinal ileus following fractured ribs is a rare condition; to date only five cases have been reported.

(2) Ten additional cases of ileus complicating fractured ribs are described.

(3) The mechanism by which this dilatation of the small bowel occurs is not clearly understood.

(4) Irritation of the dorsal sympathetic ganglia and splanchnic nerves appears to be the most plausible explanation. This irritation may be accomplished by displacement of the head of the rib or a proximal fragment, retropleural edema or hematoma in the paravertebral area, or reflex stimulation of the splanchnics through the peripheral abdominal or thoracic nerves.

(5) Experimental stimulation of the splanchnic nerves produces relaxation and cessation of movement of the small bowel.

(6) In eight of ten cases of ileus following rib fracture, the fracture was within 5 cm. of the lateral vertebral border. This proximity to the thoracic sympathetic ganglia and splanchnic nerves suggests that irritation of these nerves as a result of trauma does occur.

(7) If the presence of a ruptured intra-abdominal viscus can be ruled out, this condition is best treated conservatively without operation.

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THE EFFECT OF THE SULFONAMIDES ON THE PREVENTION OF EXPERIMENTAL BRAIN ABSCESS

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BUCY,[1] GRANT,[2] AND ROWE[3] have used the sulfonamides in the treatment of brain abscesses as an adjunct to surgical therapy. Clinical data suggested that when these compounds are used the incidence of meningitis is reduced and the spread of the encephalitis following operation may perhaps be controlled. In the present communication we are reporting on the use of the sulfonamides in the prevention of the experimental brain abscesses.

Experimental Method.—Healthy mongrel dogs were used in these experiments. In the present studies the technic for abscess production was the same as previously reported,[4] except that the dose of bacterial inoculum was increased. This was done to insure death of the control dogs within a short period (24 to 72 hours), following introduction of the organisms.

At the start of this experiment one of the sulfonamides, sulfapyridine, was administered through various channels: (1) Intravenous injection of 0.1 Gm. per kilogram of the sodium salt, twice a day; (2) the daily intravenous injection of 0.1 Gm. per kilogram of the sodium salt and the introduction intraperitoneally of 0.4 Gm. per kilogram of an emulsion of sulfapyridine prepared by the use of sonic vibrations[5]; and (3) 0.5 Gm. of sulfapyridine per kilogram by mouth daily given in a single dose.

Blood was withdrawn each morning before giving an additional dose of the drug, and determinations were made on these samples of the blood concentration of the drug being used. The oral administration was found to give the most satisfactory results and was used in most of the experiments. The dose of sulfanilamide, sulfapyridine, and sulfathiazole was 0.5 Gm. per kilogram daily, and that of sulfadiazine 0.25 Gm. per kilogram daily. All of these compounds were started two hours following the cerebral injection of the bacterial inoculum unless otherwise stated. All treated dogs received a course of five days of treatment.

Sulfanilamide, sulfathiazole, sulfapyridine, and sulfadiazine were used against pneumococci Type-III, hemolytic streptococci and *Staphylococci aureus.* The organisms were obtained from the heart blood of living mice and were cultured for 12 hours. Control experiments were carried on simultaneously with each chemotherapeutic experiment.

Results.—The data on mortality and survival obtained in these experiments are given in Table I. It can be seen that when the bacterial inoculum consisted of pneumococci, sulfapyridine and sulfadiazine provided complete protection against abscess formation when chemotherapy was begun two hours

following injection of the bacterial inoculum. Sulfapyridine protected 75 per cent of the dogs from abscess formation even though therapy was not begun for 17 hours following the injection of the bacterial inoculum. The mortality of the control groups was 100 per cent. While sulfanilamide protected 66.0 per cent of the dogs, sulfathiazole was only moderately effective.

Sulfapyridine was not used following the injection of *Staphylococcus aureus*. When this organism was injected, sulfanilamide, surprisingly, seemed slightly more effectual than the other compounds which were used.

TABLE I

	Pneumococcus Type-III		Staphylococcus Aureus		Hemolytic Streptococcus	
Drug	No. in Group	Per Cent Survival	No. in Group	Per Cent Survival	No. in Group	Per Cent Survival
Sulfanilamide:						
Treated.....	6	66.0	4	100.0	4	75.0
Control.....	4	0.0	4	0.0	4	25.0
Sulfapyridine:						
Treated.....	12	100.0			10	20.0
	4	75.0*				
Control.....	12	0.0			10	0.0
	4	0.0				
Sulfathiazole:						
Treated.....	6	33.0	4	75.0	4	75.0
Control.....	4	0.0	4	0.0	4	25.0
Sulfadiazine:						
Treated.....	7	100.0	4	75.0	4	50.0
					8	37.5†
Control.....	3	0.0	4	0.0	4	0.0
					4	0.0

* Treatment began 17 hours after inoculation.

† Treatment began six hours after inoculation. No latent abscesses have developed; and some dogs have lived six months.

Sulfapyridine and sulfadiazine were less effectual against the formation of abscess where hemolytic streptococci were used than the other compounds; although sulfadiazine provided some protection even when therapy was begun as late as six hours following injection of the bacterial inoculum.

In Chart 1 are recorded the mean blood levels of the drugs of the treated dogs during the first four days of therapy. It is interesting to note the high mean levels which were maintained when sulfadiazine was used. When sulfapyridine and sulfathiazole were administered orally a number of the dogs vomited at a variable period of time after the introduction of the drug into the stomach through a gastric tube. This rarely occurred with sulfanilamide and never occurred with sulfadiazine.

The mean blood concentrations of the treated dogs which died were in every instance within the range of the mean blood concentrations of surviving dogs, except for the dogs which died while receiving sulfadiazine. Even so, these dogs maintained a mean blood concentration of 20.8 mg. per cent until the time of death. The minimal effective blood concentrations of these compounds were not determined.

Discussion.—The high sulfadiazine blood level was maintained on a

smaller dose per kilogram of body weight than any of the other sulfonamide compounds which were studied. The absence of low blood concentrations in any of the dogs which received sulfadiazine was, we believe, an expression of the ease with which this drug was tolerated when orally administered.

Comparison of the compounds shows that sulfanilamide and sulfadiazine are approximately equally effective for the organisms studied. The high blood level obtained when relatively small doses of sulfadiazine were used, and the complete absence of vomiting, would suggest that this compound may be the one of choice when oral sulfonamide therapy is indicated and close supervision is not possible. This would be especially true when these compounds were being administered immediately following injury during military engagements, where a considerable period of time may elapse before the injured man is admitted to a general hospital.

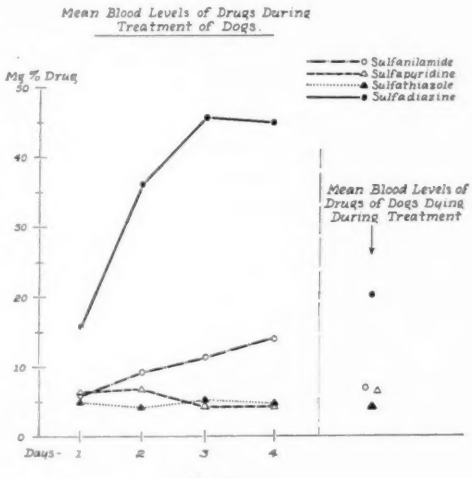

CHART 1.

The data indicate that experimental cerebral infection can be prevented or controlled in a high percentage of instances with adequate oral sulfonamide therapy.

Conclusions.—The data from these experiments indicate that sulfonamide therapy is effectual in preventing a pyogenic brain abscess following injection of pneumococcus Type-III, *Staphylococcus aureus*, and the hemolytic streptococcus into a cerebral area previously traumatized.

Sulfonamide therapy should be begun early, for the few data available suggest that with an increasing time interval between infection and the beginning of therapy the mortality also increases.

Sulfanilamide and sulfadiazine were found to be the most effective compounds.

It is suggested that intracranial infection in man, following injury, may, in part, be prevented by early and adequate sulfonamide therapy.

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THE RELATION OF HYPERTHYROIDISM TO HYPERTENSION*

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A discussion of the relation of hyperthyroidism to hypertension was presented in a previous publication.[2] The opinions expressed in that discussion were derived from a study of a total series of 265 cases of hyperthyroidism, in which 80 cases, or 30 per cent of the series, had preoperative resting systolic pressures in excess of 150; that is, in excess of a level assumed to be the upper limit of normal.

It is the purpose of the current communication to supplement the previous one with a report of an analysis of an additional 86 cases, 19, or 22 per cent, of which had resting systolic pressures in excess of 150.

Since the analytical study showed that this second series differed little from the first one, the two are discussed jointly as a single combined series. The sex-ratio was approximately four women to one man. All cases had subtotal thyroidectomies, with preoperative records of essential data as summarized in Table I. The average age was 35.5 years; the duration of toxic symptoms 12 months; and the basal metabolic rate plus 45.1. The preoperative blood pressures averaged 142/77. The systolic pressure exceeded 150 in 99, or 25 per cent of the cases; 160 in 65, or 18.5 per cent; and 200 in 13, or 3.7 per cent. In general, the cases with the higher pressures were older and had had thyrotoxic symptoms for a longer time.

Table I

Data from analysis of 351 cases of hyperthyroidism

	No. of P't's.	Per Cent of Total	Averages: Systolic Pressure	Diastolic Pressure	Pulse Pressure	B.M.R.	Age of P't's.	Duration of Toxic Symptoms. (Mos.)
Total cases studied.....	351		142	77	65	+45.1	35.5	12
Systolic over 150.....	99	25.3						
Systolic over 160.....	65	18.5	180	92	88	+41.5	43	24.5
Diastolic over 90.....	66	18.8						
Pressures over 150/90...	52	14.8						
Pressures over 160/100..	19	5.4	193	112.5	80.5	+36.2	47.5	27
Systolic over 200.....	13	3.7	228	111.5	116.5	+33	49	22.5

Assuming that 145 represents the upper limit of normal for the systolic blood pressure, all cases with pressures above this level were considered hypertensives, and follow-up observations one year or more after operation were obtained in all such cases which were available for examination. Such records were obtained in 49 cases, or approximately one-half of the group. A comparison of the resting blood pressure levels before and one year or more after operation is shown in Tables II and III.

* Read before the first meeting of the Central Surgical Association, February 28, and March 1, 1941, Ann Arbor, Mich.

The records of the 48 cases were tabulated in two groups: (1) Those in which the preoperative systolic pressure was between 145 and 170; and (2) those in which it was 170 or more.

In the first group there were 32 cases. In 24, or 75 per cent, of these the systolic pressure one year or more after operation showed some reduction from the preoperative level, and in 19 of the 24, or 60 per cent of the

TABLE II

ANALYSIS OF 32 CASES OF HYPERTHYROIDISM IN WHICH THE PATIENT HAD A PREOPERATIVE SYSTOLIC PRESSURE BETWEEN 145 AND 170

Age	Sex	Duration of Toxic Symptoms	Basal Metabolic Rate	Pathologic Condition	Preoperative Pressures		Pressures 1 Yr. or More After Operation		Reduction		Increase	
					Systolic	Diastolic	Systolic	Diastolic	Systolic	Diastolic	Systolic	Diastolic
45	F.	1 yr.	+37	Adenohyperplasia	160	72	132	68	28	4	..	..
18	F.	1 yr.	+55	Hyperplasia	155	100	119	83	36	17	..	..
39	F.	4 mos.	+34	Carcinoma	160	100	122	78	38	22	..	..
56	F.	2 mos.	+49	Adenohyperplasia	166	66	150	90	16	..	..	24
32	F.	3 yrs.	+46	Adenohyperplasia	160	106	115	70	45	36	..	..
35	F.	4 yrs.	+75	Hyperplasia	150	95	130	70	20	25	..	..
18	F.	6 mos.	+18	Hyperplasia	165	90	124	72	41	18	..	..
22	F.	4 yrs.	+59	Adenohyperplasia	160	80	140	80	20	0	..	..
46	F.	3 mos.	+28	Adenohyperplasia	160	90	168	100	..	..	8	10
38	F.	4 yrs.	+23	Adenoma	168	110	182	120	..	..	14	20
21	F.	10 mos.	+68	Hyperplasia	150	80	140	90	10	..	..	10
37	F.	2 yrs.	+17		145	100	180	100	..	..	35	0
62	F.	5 mos.	+91	Hyperplasia	150	70	150	68	..	..	..	..
46	F.	3 yrs.	+23	Hyperplasia	150	90	126	82	24	8	..	..
45	F.	.....	+41	Hyperplasia	155	80	126	80	29	0	..	..
49	F.	5 yrs.	+94	Hyperplasia	156	70	170	90	..	..	14	20
33	M.	2 mos.	+36	Hyperplasia	150	70	146	82	4	..	..	12
57	F.	1 yr.	+33	Adenohyperplasia	158	78	140	100	18	..	..	22
24	F.	3 yrs.	+37	Adenohyperplasia	155	72	132	86	23	..	..	14
47	M.	6 mos.	+54	Hyperplasia	150	90	140	75	10	15	..	..
35	F.	2 yrs.	+43	Hyperplasia	145	94	130	80	14	14	..	..
22	F.	2 yrs.	+52	Hyperplasia	152	82	125	70	27	12	..	..
34	F.	3 yrs.	+26	Adenohyperplasia	155	75	155	94	..	..	0	19
30	F.	3 mos.	+54	Hyperplasia	150	80	120	73	30	7	..	..
56	M.	3 yrs.	+29	Adenohyperplasia	150	80	150	80	0	0	..	..
25	M.	4 yrs.	+46	Hyperplasia	150	90	128	84	22	6	..	..
36	M.	3 mos.	+60	Diffuse hyperplasia	160	95	140	90	20	5	..	..
38	M.	6 mos.	+58	Diffuse hyperplasia	168	80	118	70	40	10	..	..
48	M.	10 mos.	+48	Adenohyperplasia	154	95	160	100	..	..	6	5
60	F.	14 mos.	+32	Adenohyperplasia	170	105	150	100	20	5	..	..
52	F.	8 mos.	+49	Adenohyperplasia	158	90	140	85	18	5	..	..
45	M.	2 yrs.	+32	Diffuse hyperplasia	150	85	126	75	24	10	..	..

group, there was considerable reduction; in 11 cases the pressure became normal. There was a reduction of diastolic pressure in 17 cases. Systolic pressure increased in five cases and diastolic pressure in ten cases. There was no change of pressure in two cases.

In the second group there were 16 cases (Table III). In eight of these, or 50 per cent, reductions of both the systolic and the diastolic pressure had

followed thyroidectomy and had been maintained for periods of one to five years. In four of the eight cases the pressure was nearly normal. In four cases there was an increase of pressure, in three of them an extreme increase. In two cases there was little or no change of pressure.

TABLE III

16 CASES OF HYPERTHYROIDISM WITH HYPERTENSION WITH SYSTOLIC PRESSURE OF 170 OR MORE

Age	Sex	Duration of Toxic Symptoms	B.M.R.	Pathologic Condition	Preoper. B.P.		Postoper. 1 Yr. or More		Reduction		Increase	
					Syst.	Diast.	Syst.	Diast.	Syst.	Diast.	Syst.	Diast.
62	F.	2 yrs.	+28	Adenohyperplasia	250	120	180	80	70	40	..	..
32	F.	7 yrs.	+78	Diffuse hyperplasia	200	100	120	72	80	28	..	..
47	F.	18 mos.	+43	Adenoma	182	100	142	80	40	20	..	..
25	F.	1 yr.	+63	Diffuse hyperplasia	178	80	65	50	113	30	..	..
41	F.	1 yr.	+31	Adenohyperplasia	172	90	230	124	..	..	58	34
48	F.	1 yr.	+75	Diffuse hyperplasia	170	90	164	90	6	0	..	..
26	F.	6 mos.	+25	Diffuse hyperplasia	170	90	130	85	40	5	..	..
48	F.	2 yrs.	+51	Adenohyperplasia	170	90	210	100	..	..	40	10
56	M.	2 yrs.	+55	Adenohyperplasia	170	90	180	90	..	..	10	0
58	M.	2 yrs.	+48	Adenohyperplasia	180	110	130	90	50	20	..	..
23	M.	6 mos.	+51	Diffuse hyperplasia	170	80	170	88	..	..	0	8
48	F.	9½ mos.	+60	Adenohyperplasia	230	140	210	140	20	0	..	..
68	F.	10 mos.	+32	Adenohyperplasia	190	100	138	90	52	10	..	..
52	F.	1 yr.	+45	Adenohyperplasia	240	160	200	130	40	30	..	..
31	M.	6 mos.	+68	Diffuse hyperplasia	178	100	126	70	52	30	..	..
49	M.	14 mos.	+44	Adenohyperplasia	182	115	210	120	..	..	28	5

Combining the figures from the two groups shows that in 21 cases the blood pressure was uninfluenced by relief of hyperthyroidism and either remained essentially unchanged or continued to increase. In 27, or a slightly larger number of cases, however, the blood pressure was appreciably reduced after thyroidectomy, and in 15 it became relatively normal or normal.

COMMENT.—From the data just presented two types of cases are distinguishable:

(1) A type in which hyperthyroidism and an established hypertension coexist, incidentally, in the same person as separate, unrelated entities. Usually, the hypertension is essential in type, although its severity apparently is increased by the thyrotoxic state, and some improvement may follow release from hyperthyroidism. Despite symptomatic improvement, however, the blood pressure, both systolic and diastolic, remains high and, usually, is not significantly lowered, and the hypertension continues to progress.

(2) A type in which relief of hyperthyroidism by subtotal thyroidectomy causes both the systolic and the diastolic pressure to recede promptly to a much lower, or normal, or nearly normal level, at which it remains or from which, after a period of many months, it again gradually ascends. This response suggests that thyrotoxicosis in these cases either is directly responsible for the hypertension or, more likely, precipitates or exaggerates a latent vascular disorder. It is conceivable that an inelastic or restricted vascular bed,

capable of receiving the normal cardiac output without appreciable elevation of blood pressure, would be unable to receive the increased output incident to hyperthyroidism without a sharp rise in the propelling force. Conversely, with lessening of the output by remission of hyperthyroidism the pressure required to propel the blood is diminished. In other words, this hypothesis assumes the existence of arteriolar pathologic changes which are insufficient to increase appreciably the resistance to a normal volume of blood flow but which are sufficient to prevent normal expansion as the load is increased in response to either hyperthyroidism, exercise, or the cold pressor test.

This hypothesis finds support in the response of the seven cases (three of the group in Table III, and four private cases not included in the present series) subjected to exercise and to the cold pressor test of Hines and Brown.[1] These determinations are shown in Table IV. In all cases large reductions of blood pressure had developed and been sustained after subtotal thyroidectomy.

TABLE IV

EFFECT OF EXERCISE AND OF THE COLD PRESSOR TEST ON THE BLOOD PRESSURES OF SEVEN PATIENTS ONE YEAR OR MORE AFTER SUBTOTAL THYROIDECTOMY

Case	Age	Preop. B.M.R.	Postop. Pulse	Blood Pressure				Pulse Rate	
				Preop.	Postop.	After Exercise	After Immersion of Hands	After Exercise	After Immersion of Hands
1	47	+43	76	182/100	142/80	195/95	185/105	104	82
2	58	+48	84	180/110	130/90	190/100	185/105	110	92
3	62	+28	68	250/120	180/80	230/110	230/110	100	74
4	60	+62	82	210/110	150/105	220/112	218/110	98	80
5	56	+58	72	190/115	150/108	190/120	200/124	112	72
6	31	+68	72	178/100	126/70	160/90	148/90	92	82
7	45	+52	78	190/110	140/82	162/90	170/95	102	90

After the basal level of blood pressure had been obtained, each patient was given sufficient exercise to increase the pulse rate appreciably (from 16 to 40 beats per minute), and the blood pressure was determined immediately afterward and at subsequent intervals of 60 seconds. In each instance the pressure rose to the approximate preoperative resting level. Moreover, these levels were sustained abnormally long and receded abnormally slowly. Thus, the response of blood pressure to the increased cardiac output incident to exercise was approximately the same as that recorded preoperatively during the thyrotoxic state.

Each patient was then subjected to the cold pressor test described by Hines and Brown. In accordance with their technic, the lowest or basal level of blood pressure was obtained with the subject resting supine for 30 minutes or longer. With the blood pressure cuff in place on one arm, the opposite hand was immersed in ice water (4° C.) to a point just above the wrist for 60 seconds, and readings of blood pressure were made 30 and 60 seconds after the beginning of immersion. Within 30 seconds the pressure again mounted to approximately the same level which followed exercise. In the light of the

studies of Hines and Brown, the reaction of the blood pressure in these patients to the cold pressor test was excessive and abnormal, as is that in all subjects afflicted with essential hypertension. The studies of these investigators showed that in addition to the persons with hypertension there is a group of persons who do not have hypertension but do give excessive reactions to the cold pressor test. Persons in this group they designated "hyperreacting normals," and they stated the belief that this excessive reaction indicates a latent quality and a likelihood of subsequent development of hypertension. On this basis it may be reasoned that my patients had potential if not real essential hypertension and that the latent factor had been precipitated or exaggerated by thyrotoxicosis.

It is interesting that in each of these seven cases there was a familial history of hypertension.

CONCLUSIONS

(1) As a physiologic response to hyperthyroidism, the systolic blood pressure is usually slightly elevated. It recedes to the normal level with relief of hyperthyroidism.

(2) In this series of 351 cases, hyperthyroidism was associated with unquestionable essential hypertension (systolic pressure above 170) in approximately eight per cent, and with elevations of the systolic pressure above the physiologic level (above 150) in 25 per cent. On the basis of changes of blood pressure following relief of hyperthyroidism, two types of cases are discernible: (A) Cases with fixed or established essential hypertension, in which the blood pressure and the course of the vascular disease are not significantly influenced by relief of hyperthyroidism; and (B) cases with latent or labile essential hypertension, in which the blood pressure shows considerable reduction after relief of hyperthyroidism or approaches a normal level and maintains this level for a period of months or years. In many cases of the second type the pressure is observed subsequently to ascend. In these cases there is excessive response in blood pressure to exercise and to the cold pressor test of Hines and Brown. It is suggested that the relation of hyperthyroidism to hypertension in these cases is provocative, and that hyperthyroidism merely precipitates or exaggerates hypertension which is latent.

It is further suggested that in both types there is arteriolar disease, differing only in degree. In the first type the disease is more advanced, rendering the vascular bed inadequate for even a normal volume of blood flow. In the second type the disease may be designated as pretensive hypertension, which progresses to the condition of the first type with the advance of time.

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METASTIC TUMORS IN THE BREAST

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NO DISEASE is more full of surprises and less amenable to tradition than malignant tumors. They defy any classification or precedent. Hence the importance of continuing clinical investigation and reporting new phenomena.

Tumors of the breast are universally accepted as being primary in origin. This clinical observation is in accordance with the teaching of Virchow, that organs which are frequently the site of primary tumors are seldom affected by metastatic growths.

That metastatic tumors in the breast do occur was shown by Dawson,[1] in 1936, when he reported a case of gastric carcinoma with metastases to both breasts, proven histologically from autopsy material. He tabulated a series of ten cases collected from the literature. There have been no other reports of metastatic tumors of the breast up to the present writing.

Dawson confines metastatic mammary tumors to "those recorded instances where clinical and microscopic data point more or less to primary growths in another site."

Two such proven cases were admitted to the Brooklyn Cancer Institute. One case had its origin in an hypernephroma; the other, in a melanoma of the right forearm.

CASE REPORTS

Case 1.—Hosp. No. 1680: M. S., white, female, age 43, was admitted to the Brooklyn Cancer Institute, October 8, 1938, complaining of pain in the right side of the abdomen and loss of 20 pounds in three months. Four months previous to admission (June, 1938) she developed a cough with occasional bloody sputum. In July, 1938, she was treated for bronchitis and pleurisy. A short time later she developed pain in the right lower quadrant and was admitted to a private hospital where her appendix was removed. After ten days she was discharged. Two weeks later she reentered the same hospital, still complaining of pain in the right lower quadrant. At this time examination and roentgenologic studies revealed "neoplasm of the lungs, hydronephrosis, and ptosis of the right kidney." She was then referred to the Brooklyn Cancer Institute for roentgenotherapy.

Physical Examination.—The patient was an emaciated, chronically ill female. Temperature 100° F., pulse 120, respiration 20, blood pressure 168/60. Both breasts were symmetrical, of moderate size, and slightly pendulous. The skin was smooth and freely movable. The nipples were of equal size, and were not retracted or inverted; they showed no discharge. Deep in the center of each breast a nontender, irregular, firm tumor was palpated, measuring about 3–4 cm. in diameter, attached to the underlying structures and only slightly movable. The tumor in each breast appeared to be the same size and shape, and symmetrically placed in the center. There were no palpable nodes in either axilla or supraclavicular regions. The patient stated that the breasts "never bothered" her.

The heart was somewhat enlarged; an apical systolic and double aortic murmur

was present, which was transmitted to the vessels of the neck. The lungs showed dulness at both bases and right interscapular areas, with diminished tacticle fremitus and breath sounds. A few scattered moist râles were present.

FIG. 1.—Case 1: Photomicrograph showing anaplastic cells of hypernephroma. (×800)

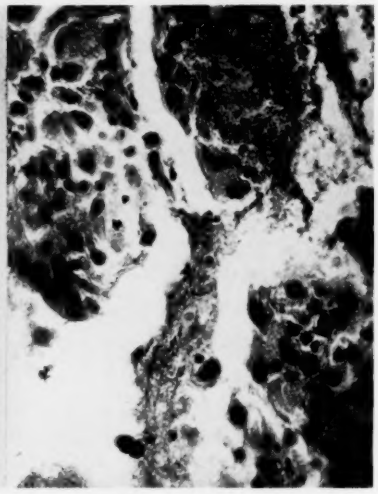

FIG. 2.—Case 1: Photomicrograph showing anaplastic cells of metastatic hypernephroma in the breast. (×800)

FIG. 3.—Case 1: Photomicrograph showing metastatic hypernephroma of the breast. (×200)

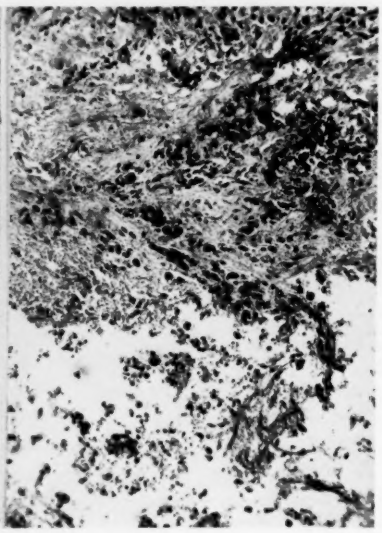

FIG. 4.—Case 2: Photomicrograph showing metastatic melanocarcinoma of breast. (×200)

The abdomen was slightly distended. The liver was enlarged to two fingers breadth below the costal margin. A large, firm mass was felt below the liver, corresponding to the region of the right kidney, which was very painful on palpation. There were no other palpable masses. The spleen was not enlarged. Pelvic examination revealed no evidence of pathology.

Roentgenographic examination of the chest showed multiple metastatic nodules in both lungs. A pyelogram showed a tumor of the upper half of the right kidney, associated with hydronephrosis. Urine: Albumin 2 plus, with 43–61 red blood cells per field and many squamous epithelial cells. Blood chemistry: Urea 36 mg., creatinine 1.2, sugar 100 mg. Blood examination: Red cells 2,900,000, with 42% hemoglobin; white cells 33,000, with 84% polymorphonuclear leukocytes, 13% lymphocytes, and 3% eosinophils. Blood Wassermann, negative.

Both breast tumors were removed under local anesthesia for diagnosis. They were found to be, histologically, the same—metastatic hypernephroma (Path. No. 1505). The patient received supportive treatment, but her condition became progressively worse and

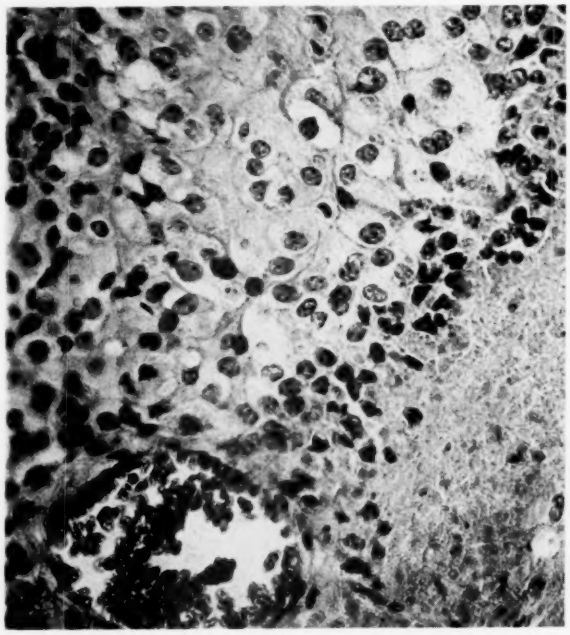

FIG. 5.—Case 2: Photomicrograph showing malignant characteristics of the cells. (×800)

she died October 28, 1938. Autopsy was not permitted, except for removal of a portion of the primary tumor in the abdomen. The pathology of this tumor proved to be the same as that of the tumors of the breasts. Confirmation of this diagnosis was made by Dr. James Ewing. Both tumors proved to be of renal origin.

Case 2.—Hosp. No. 7937: W. S., white, male, age 42, was admitted to the Brooklyn Cancer Institute, June 19, 1935, complaining of a lump on the right chest and right elbow. About two years previous to admission he had had a "warty" growth removed from the right forearm. About six months before admission he noticed a lump on the right elbow and right chest, which grew progressively larger. His family history and past history were irrelevant. He had lost ten pounds within the last year.

Physical Examination.—The patient was a well-developed white male, weighing 158 pounds, and was 5′ 5″ in height. Not acutely or chronically ill. Temperature 99° F., pulse 80, respiration 18, blood pressure 120/90. A palpable node, the size of a walnut, was present in the right epitrochlear region. In the upper outer quadrant of the right mammary region was a large, firm tumor, the size of a grapefruit, extending from the upper part of the nipple to the anterior axillary line, and involving the lower outer two-thirds of the pectoral region. The skin over the tumor was stretched, but not adherent,

and the tumor appeared to be fixed to the pectoral muscles. The right nipple was somewhat larger than the left, freely movable, and without any evidence of gross pathology.

The heart sounds were regular in rate and rhythm, and no murmurs were heard. The lungs did not show any clinical evidence of pathology, but roentgenologic examination revealed a nodule, 2–3 cm. in diameter, in the left lung, at the level of the fifth rib. The abdomen was free from any palpable tumor, but the liver was enlarged to 2 cm. below the costal margin. This enlargement of the liver was also noted on a plain roentgenogram of the abdomen.

The blood chemistry and the blood count were within normal limits. The blood Wassermann was negative. The urine was not pathologic.

On July 11, 1935, a radical right mastectomy was performed, with excision of the epitrochlear node. The node was reported, by Dr. S. H. Polayes, as metastatic melanocarcinoma. The detailed gross and microscopic description of the breast by Dr. Polayes is as follows:

Pathologic Examination.—Gross: Path. No. 12.366: "Specimen a section of breast with a triangular piece of skin, about 14 cm. in greatest diameter, attached. It is also accompanied by pectoral muscle and fascia. The mass in the breast measures about 15 cm. in greatest diameter; is lobulated and discolored dark brown except for a few projecting lobules which are gray in color and a few others of blue discoloration. The cut-surface presents areas of necrotic brown tissue. There is no direct continuity between the mass and the overlying epidermis.

Microscopic: "The breast tissue is the seat of discrete, fairly well-circumscribed areas of malignant epithelial cells, embryonal in character, many of which are filled with brown pigment. The tumor tissue cannot be traced to the breast structures. The ducts of the breast are distended and filled with large, pale cells of lacteal origin. *Pathologic Diagnosis:* Metastatic melanocarcinoma."

Various laboratory tests of the tumor extract were positive for melanoma.

The patient made an uneventful operative recovery, and was followed in the clinic until he died at his home in September, 1935.

SUMMARY

(1) Although tumors of the breast are universally accepted to be primary in origin, metastatic tumors in the breast do occur.

(2) Ten cases have been reported in the literature up to this writing.

(3) Two additional cases are here reported, one of renal origin, the other arising in a melanoma of the forearm.

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NEOPLASMS OF THE BONY THORACIC WALL

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TUMORS involving the thoracic wall and especially those arising from the ribs and sternum have been the subject of a number of scientific papers during the last 60 years. Because of the relative infrequency of primary neoplasms of the ribs and sternum, many reports of single cases with short periods of follow-up have appeared. The earlier writers were concerned with the dangers of open pneumothorax during operation, and Parham,[60] in his notable contribution divided the collected, and his two personal cases, into groups with and without open pneumothorax at operation. With the present-day methods of administration of inhalation anesthetics with closed systems, and the use of positive pressure anesthesia, when necessary, or rhythmic pulmonary insufflation, open pneumothorax is no longer an operative danger.

The ribs and sternum are not common sites of primary tumors of bone. Among 57 osteogenic sarcomata reported by Campbell[15] only one originated in a rib, while one osteogenic sarcoma out of 41 studied by Pfahler[62] arose in a rib. Meyerding[55] discussed 100 cases of osteogenic sarcoma, three of which were of costal and three of sternal origin. Campbell[14] reported one case of Ewing's sarcoma of a rib among 23 cases, and Desjardins, Meyerding, and Leddy[20] one of a rib among 42 proven instances of Ewing's sarcoma.

A number of efforts have been made to collect the available reported cases of tumors of the thoracic wall. In 1933, Hedblom[39] gathered 291 cases, including those reported by himself[37] in 1921, and added 22 additional personal cases. In reviewing the original reports of the collected tumors in his[39] paper of 1933, it was noted that histologic diagnoses had not been made on a number of the tumors, some of which had been treated by roentgenotherapy, without biopsy. In his earlier paper Hedblom[37] included a number of instances of tumors metastatic to the bony thoracic wall, and in both papers did not present, in detail, all his own cases, but gave only statistical data concerning the majority of them. It is not possible, moreover, in many of the earlier reports to evaluate the nature of the neoplasm described. The cases of Fort[25] and Gatewood,[26] for example, were reported as sarcomata but are now listed by the Bone Sarcoma Registry of the American College of Surgeons as instances of benign giant cell tumor (Samson and Haight[68]). Such corrections of diagnoses, in the light of new knowledge, are unfortunately rarely available.

In spite of the difficulty of determining accurately the nature and number

of earlier reported cases of tumors of the bony thoracic wall, it seemed to be of value to collect the cases reported since Hedblom's[39] study of 1933* and to present them with 15 cases from the University of Michigan Hospital. The recent advances in the technic of thoracic operations, it was thought, should be reflected in improved clinical results. No tumor described in the literature without apparent adequate histologic study has been accepted. The case of Smith[70] is not included since two different diagnoses were made; and the chondroma reported by Jitsuiki[48] is omitted since the description was exceedingly brief. Cases may appear twice in the literature as in the reports of Allessandri[1] and Vitale.[77] Myeloma has not been considered. Batts[4] has presented 40 cases of multiple myeloma from the University of Michigan Hosptial, 68 per cent of them involving ribs.

Diagnosis.—The important symptoms of neoplasms of the bony thoracic wall are tumor and pain. Severe pain is often associated with malignant tumors. Among the patients presented in this report, fever, weight loss, dyspnea, palpitation, mild supposed gastro-intestinal distress, and pleurisy occurred only rarely. Pleural effusion was present in only two patients, both of whom had Ewing's sarcoma.

The most important means of diagnosis of tumors of the ribs and sternum is the use of roentgenograms, the value of which, in certain cases, is increased by special positioning of the patient, fluoroscopy, and artificial pneumothorax. Jacobeus and Key,[45] and Matson[54] have shown that inspection of the pleural cavity, after pneumothorax, with the thoracoscope may be useful in establishing the correct diagnosis and the extent of the thoracic wall lesions. Biopsy and histologic study of the removed tissue may be necessary for a correct diagnosis. Obviously, the history of the case and the physical findings are important diagnostic aids.

Differential diagnosis requires a consideration of various lesions of the thoracic wall, pleura, lung, and mediastinum, including aneurysm, osteomyelitis, gumma, cold abscess, encapsulated empyema, empyema necessitatis, bronchial carcinoma (which may directly involve the thoracic wall), echinococcus cyst, and mediastinal tumors.

Treatment.—The data assembled for this report have given little evidence that radiologic therapy is of great value in the treatment of tumors of the thoracic wall. In two instances of benign giant cell tumor favorable results were obtained; Neil's (Samson and Haight[68]) patient was apparently cured by the use of radium, and roentgenotherapy caused the regression of the tumor in Hilt's[42] patient. A striking palliative result was obtained by roentgenotherapy in a case of Ewing's sarcoma reported by Bergstrand;[6, 7] in this patient, very extensive pulmonary metastases disappeared after treatment on two occasions. Death occurred one year after the second period of therapy. Except for these three favorable instances there are no reports of successful radiation therapy for bony thoracic wall tumors since 1933.

* The Quarterly Cumulative Index Medicus was available to March, 1940—(Vol. 27, No. 1).

Operative removal is the best means of therapy for tumors of the bony thoracic wall. The results of treatment by surgical means are dependent upon the nature of the tumors and the adequacy of their removal. The varying results of treatment of different types of tumors are discussed later in the article. All operations for tumors of the ribs and sternum should be carefully planned for adequate removal with resection of sufficient bony and soft parts. Attempts to excise tumors of the ribs and sternum extrapleurally, lead to partial removal with recurrence, the only too frequent result. The failure of improper resection of a tumor is well illustrated by Cabot Case No. 24212[13]—four excisions of the tumor preceded the final operation for its removal, which was followed by the discovery of metastases in the lung. This tumor, which recurred four times before metastases became apparent, was considered benign at the time of the first four operations. With the employment of proper methods of anesthesia the thoracic cavity should always be opened at operation. Provision must be made for airtight closure of defects in the thoracic wall after removal of bony structures. Janes[46] has described the replacement of the anterior portion of the second rib by use of part of the adjacent third rib as a pedicled graft; in this manner he assured the stability of the anterior thoracic wall following the removal of a tumor of the second rib.

Remarkably extensive resections of the sternum, with opening of both pleural cavities, have been successfully performed by Heuer[41] and John Alexander (Authors' Case 2). Haight (Authors' Case 9) also resected the *gladiolus sterni* and opened the left pleural cavity for chondrosarcoma. Nissen[57] removed a large osteogenic sarcoma with long lengths of four ribs anterolaterally, and a generous portion of the upper lobe of the lung infiltrated in continuity by the tumor; the patient recovered from the operation without especial difficulty. Hautefort[36] described the successful removal of a round cell sarcoma with the third, fourth, and fifth ribs and the middle lobe of the right lung from a four-year-old child; the tumor was adherent to, but had not infiltrated the lung.

Case 1 of this article exemplifies the treatment of a costal tumor by a properly planned operation. Following the admission of the patient to the University of Michigan Hospital, roentgenograms were made in oblique projections after the induction of artificial pneumothorax to obtain information in addition to that furnished by postero-anterior roentgenograms. These films demonstrated that the tumor, which was considered to be an osteogenic sarcoma, arose from the posterolateral portion of the left sixth rib and that it was not adherent to the lung. Fluoroscopic examination was also carried out. At operation a parascapular incision was carried well forward below the tip of the scapula, the trapezius and rhomboideus major and latissimus dorsi muscles were divided, and the scapula was retracted. The skin and muscles were divided at different levels in order to avoid overlying suture lines following closure of the wound. The tumor was not adherent to these muscles. The sixth rib was divided at the level of the vertebral transverse process and

the pleural cavity was opened posteriorly. A long length of the rib was removed with the adjoining intercostal muscles, which were divided close to the fifth and seventh ribs. Even though the approximation of the intercostal structures was not possible, airtight closure of the large wound was readily obtained by careful suture of the extracostal muscles, the subcutaneous tissues, and the skin, after reexpansion of the lung. Examination of the tumor demonstrated the absence of infiltration of the intercostal muscles—the histologic diagnosis was osteoma. Every care had been taken, however, to secure the complete removal of a tumor considered to be malignant before operation.

The treatment of metastatic tumors of the lung secondary to primary tumors of the ribs and sternum has been quite unsatisfactory, as might be expected, since the primary tumors themselves have been resistant to roentgenotherapy. The favorable result of treatment of one metastatic Ewing's sarcoma has been mentioned. Recently, Churchill[13] has successfully removed the lower lobe of the right lung with an adjacent portion of the diaphragm for a metastatic osteogenic sarcoma; the primary site was in the left fourth rib. This represents the first reported operative treatment of an hematogenous metastatic pulmonary tumor with the primary focus in a rib.

For this article, a classification of tumors based upon histologic structure has been used. Zinninger[78] proposed a clinical classification of neoplasms of the thoracic wall, dividing them into tumors arising from the deep structures of the thoracic wall and partially intrathoracic, those arising from the superficial structures but fixed to the deep structures, and those arising within the thorax and presenting through the thoracic wall. The primary interest of the present discussion is in the treatment of tumors involving the ribs and sternum. It is often difficult, clinically, to draw a sharp line between neoplasms arising primarily in the bony thoracic wall and those primary in the soft tissues involving the ribs and sternum secondarily. Probably none of the cases of fibrosarcoma, neurofibroma, schwannoma, lymphosarcoma, and Hodgkin's disease, to be presented, originated in any case in the bony thoracic wall in spite of their intimate association with it.

In order that a proper evaluation of the results of therapy of the different histologic types of tumors involving the ribs and sternum may be obtained, the collected cases, together with those from the University of Michigan Hospital, have been tabulated. The results of treatment vary strikingly in the benign and malignant groups. Unfortunately, long periods of follow-up are available for only a comparatively small percentage of the cases. In many instances reports were made shortly following successful operations. A comparison is available from these data of the operative mortality in treatment of benign and malignant tumors and to some extent of the late results of treatment.

OSTEOMA

Table I lists data concerning five cases of osteoma of the ribs, including one fibro-osteoma and one chondro-osteoma. There were four women and

one man, with ages varying from 24 to 49 years. Tumor and pain were the only symptoms, but they occurred together in only one case. The pain of the patient of Klapp[51] was caused by pressure of a tumor of the first rib on the brachial plexus. In Case 1 of this report the pain was of a pleuritic type and was associated with a temperature of 101° F.; pulmonary tuberculosis was suspected and roentgenographic study demonstrated the tumor, which could not be palpated. The duration of symptoms varied from one month to 30 years. All five tumors, the largest 25 cm. in diameter and the smallest 5 cm. in diameter, were successfully removed at operation. Follow-up data are available on only one patient, who is well two years after operation.

TABLE I

OSTEOMA

Author	Sex	Age	Site	Size	Initial Symptoms	Other Symptoms	Duration	Treatment	Result	Histologic Diagnosis	Remarks
(1) Jeanneney and Chabe[47]	F	49	11th rib	Billiard ball	Pain	—	4 yrs.	Removal, with 11th rib	Survived operation	Osteoma	Pain followed trauma
(2) Andrus[2]	M	42	5th rib	25 cm. in diameter	Tumor	—	30 yrs.	Removal	Survived operation	Osteoma	Tumor followed fracture
(3) Klapp[51]	F	28	1st rib anteriorly	Duck egg	Tumor	Pain in brachial plexus distribution	18 mos.	Removal, with 1st rib	Survived operation	Fibro-osteoma	
(4) Guitierrez[30]	F	24	3rd rib anterolaterally	5 cm. in diameter	Pain	Tumor	1 mo.	Removal, with 3rd rib	Survived operation	Chondro-osteoma	
(5) Authors' (Case 1)	F	26	6th rib posterolaterally	8x5x5 cm.	Pain	Temp. 101° F.	2 mos.	Removal, with 6th rib	Well 2 yrs. later	Osteoma	

Author's Case 1.—M. B., white, female, age 25, was admitted July 20, 1938. For two months she had suffered with mild pleuritic pain beneath the left breast. One week previous to admission she had consulted a physician, who found her temperature to be 101° F. A tuberculin test was positive; and a roentgenogram revealed a tumor arising from a rib on the left. Physical examination disclosed a moderately obese white woman, with compensated rheumatic heart disease with mitral stenosis and insufficiency. There was no palpable evidence of a costal tumor. Roentgenograms (Figs. 1 and 2) demonstrated a well-localized, dense tumor with areas of translucency involving the axillary portion of the sixth rib. The tumor was thought to be an osteogenic sarcoma, with osteochondroma and osteoma as possibilities. A left pneumothorax was induced July 21, 1938. The tumor was removed July 23, 1938, according to the operative procedure described already. A satisfactory recovery from operation ensued, with air and fluid being aspirated on several occasions from the left pleural cavity. The patient was discharged two weeks after operation.

The tumor (Fig. 3) was described as an osteoplastic growth on the pleural surface of a rib, measuring 6x3x3 cm., with several cystic foci. Microscopic examination, after decalcification, showed dense bone with fatty marrow and some proliferating bone. *Pathologic Diagnosis:* Osteoma. The patient is well in July, 1940, two years following removal of the tumor.

CHONDROMA

In Table II are grouped 16 cases of chondroma of the ribs and sternum. Eleven occurred in men, four in women, and one in a three and one-half months'-old boy. The ages of 15 patients ranged from 21 to 55 years. In addition to the common symptoms of tumor and pain, dyspnea, mild digestive symptoms, and loss of weight each occurred once. One patient had no symptoms referable to the tumor, which was discovered by fluoroscopic examina-

FIG. 1. FIG. 2.

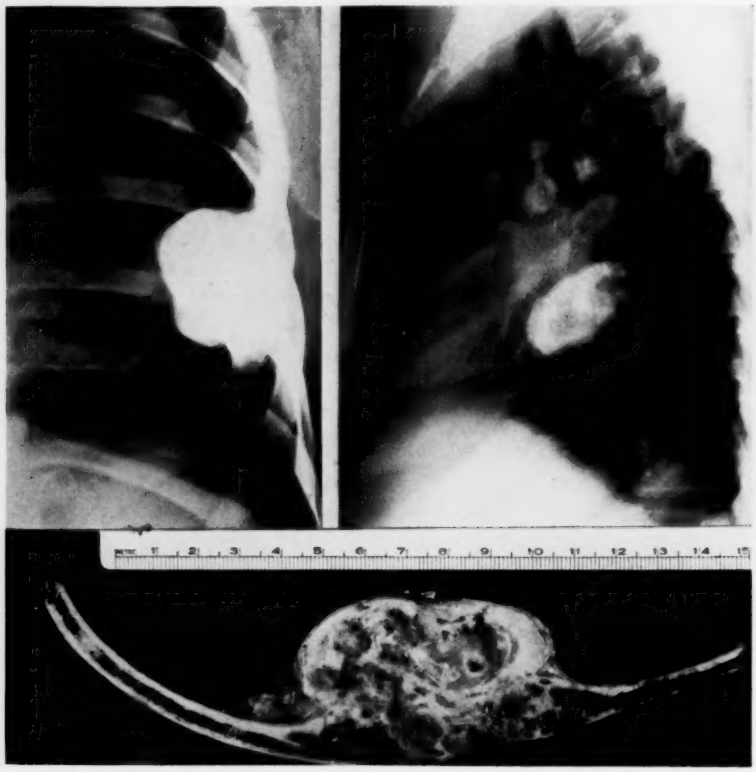

FIG. 3.

FIG. 1.—Case 1: Postero-anterior roentgenogram of osteoma of left sixth rib.
FIG. 2.—Case 1: Lateral roentgenogram of osteoma of left sixth rib.
FIG. 3.—Case 1: Longitudinal section of osteoma of rib.

tion during an industrial employees' health examination. With one exception, a tumor two centimeters in diameter, the chondromata were of moderate or large size. All 16 neoplasms were removed surgically, with one postoperative death following removal of a football-sized tumor. The operative mortality in this group was 6.2 per cent. Two resections were considered incomplete by the surgeons; the two patients are reported living and well, one and five years, respectively, following operation. Eight additional patients are living and well, eleven, seven and one-half, four, three and one-half, two, and one and two-thirds years, and six and five months, respectively, after operation.

Follow-up data after operative recovery are not available on five patients. In only one case was roentgenotherapy administered after operation.

The chondromata are often mentioned as tumors likely to become malignant after years of benign growth. Such a change may have occurred in the cases of Auchincloss,[3] whose tumor was of seven years' duration at the time of treatment; at autopsy a nodule of similar structure to the costal osteochondroma was found in a lung. The tumor of Golla's[29] patient was of 14 years' duration, without malignant change in spite of recurrence, while in the cases of Sokolov,[71] Harper,[32] and Santy[69] the tumors were of ten, six, and four years' duration, respectively, before treatment.

FIG. 4.—Case 2: Lateral roentgenogram of recurrent chondroma of *gladiolus sterni*; the posterior projection of the tumor against the heart is shown.

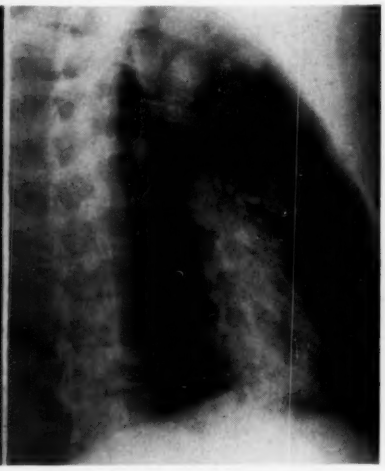

FIG. 5.—Case 2: Oblique roentgenogram of recurrent chondroma of *gladiolus sterni*.

Author's Case 2.—A. O., white, male, age 34, was admitted January 1, 1932. About one year previously he had noted a dull ache over the lower portion of the sternum and shortly afterwards a small nodule appeared in this region, which was hard and which grew steadily. October 3, 1931, following a biopsy, a growth the size of a baseball was removed from the sternum, leaving only a thin shell of bone posteriorly, from which tumor tissue was curetted. The neoplasm promptly recurred and grew rapidly. On examination the patient presented a mass over the sternum from the level of the second rib to the fourth interspace, measuring 5x3x1 inches. The tumor was irregular with rounded nodules; it was rubbery at the upper pole, but hard and fixed inferiorly. To the right of the midsternal line was a four-inch vertical scar centered at the level of the third interspace. Roentgenographic examination (Figs. 4 and 5) showed a tumor involving the middle third of the sternum, projecting posteriorly against the heart as well as anteriorly; there was irregularity in the density of calcification in the tumor. A diagnosis of osteochondroma was made. A biopsy specimen showed a cellular chondroma.

Operation.—January 13, 1932: An incision from the suprasternal notch to the xiphoid was made with excision of the soft tissue over the tumor. The right third and fourth cartilage were resected to afford access to the mediastinum. The tumor, which was adherent to the right pleura, was dissected free from the pericardium and other mediastinal structures after division of the cartilages from the third to seventh, bilaterally. Both

TABLE II

CHONDROMA

Author	Sex	Age	Site	Size	Initial Symptoms	Other Symptoms	Duration	Treatment	Result	Histologic Diagnosis	Remarks
(1) Sorrel and Oberthur[72]	M	11	2nd rib anteriorly	Large	Tumor	—	—	Partial removal	Well 1 yr. later	Chondroma	Tumor adherent to great vessels and pericardium
(2) Potvin[64]	M	26	10th rib anteriorly	Child's head	Mild digestive symptoms	Tumor; loss of weight	3 mos.	Removal, with 10th rib	Survived operation	Chondroma	
(3) Folliasson and Blanchard[23]	M	3½ mos.	6th rib at angle	5x5x5 cm.	Tumor	—	1 mo.	Removal, with 6th and 7th ribs	Survived operation	Chondroma	
(4) Auchincloss[3]	M	23	7th to 10th rib anterolaterally	Football	Tumor	Pain and dyspnea	7 yrs.	Removal, with two-stage operation	Postoperative death	Osteochondroma	Similar nodule found in lung at autopsy; metastatic lesion?
(5) Sokolov[71]	F	37	8th to 10th ribs and cartilages	Fist	Tumor	Pain	10 yrs.	Removal, with 8th to 10th ribs	Discharged from hospital well	Chondroma	
(6) Moura and Rodrigues[56]	M	21	1st rib posteriorly	Orange	Tumor	—	4 mos.	Removal, with 1st rib followed by x-ray therapy	Well 2 yrs. later	Osteochondroma	Presented in neck
(7) Santy[69]	M	38	3rd and 4th ribs anteriorly	Orange	Tumor	Pain	4 yrs.	Removal, with 3rd and 4th ribs	Survived operation	Chondroma	
(8) Golla[29]	F	55	3rd and 4th ribs anteriorly	Child's head	Tumor	Pain	9 yrs.	Previous incomplete removal, with 3rd-4th ribs; extensive operation to remove recurrent tumor 5 yrs. later	Recurred in 2 yrs., and continued to grow. Well 5 mos. after 2nd operation	Chondroma	14 yrs. total duration

(9) Harper[32]	F	17	4th rib and cartilage	5x4 cm.	Tumor	—	1 yr.	Removal, with 4th rib and cartilage	Well 6 mos. later	Chondroma	
(10) Harper[32]	M	41	6th rib anteriorly	10x3x3 cm.	Pain	—	6 yrs.	Removal	Well 3½ yrs. later	Probably chondroma	Pain referred to upper abdomen. Had been treated for gallbladder disease. Diagnosis made during industrial chest survey
(11) Janes[46]	M	30	3rd rib and cartilage	7x5 cm.	—	—	—	Removal, with rib and cartilage	Survived operation	Chondroma	
(12) Janes[46]	M	40	9th rib antero-laterally	Orange	Pain	Tumor	2 yrs.	Removal, with 9th rib and cartilage	Well 11 yrs. later	Osteochondroma	
(13) Authors' Case 2	M	34	*Gladiolus sterni*	12x6x6 cm.	Pain	Tumor	1 yr.	Previous partial removal, resection with *gladiolus sterni*	Well 7½ yrs. later	Chondroma	Both pleural cavities opened during operation. Recurrence in costal cartilage; widely removed
(14) Authors' Case 3	M	47	7th rib at head and neck	Orange	Pain	Tumor	3 mos.	Incomplete removal, with 6th to 9th ribs	Well 5 yrs. later	Chondroma	
(15) Authors' Case 4	M	26	*Gladiolus sterni* at junction with manubrium	2x2x2 cm.	Tumor	Pain	6 mos.	Removal	Well 4 yrs. later	Chondroma	Exceptionally early case
(16) Authors' Case 5	F	55	10th rib	9½x8 cm.	Tumor	Pain	1 yr.	Removal, with 9th, 10th, 11th ribs	Well 20 mos. later	Osteochondroma	

pleural cavities were entered, and the pleural openings were later closed with catgut sutures. The sternum was divided just below the manubrium and above the xiphoid. The pectoralis major muscles, which had been mobilized, were sutured together and the skin closed without drainage.

Following operation the right lung was collapsed about 50 per cent and the left only slightly. Fluid developed in the right pleural cavity, which became purulent and was drained, with rib resection, February 16, 1932. Wound infection occurred and involved the seventh and eighth cartilages, which were resected in part with some of the xiphoid May 9, 1932. The patient was discharged May 13, 1932, with the empyema and operative wounds draining.

The tumor, which is illustrated in longitudinal section (Fig. 6), was again shown, histologically, to be a chondroma. The patient returned August 13, 1932, with a tumor

FIG. 6.—Case 2: Longitudinal section of recurrent chondroma of *gladiolus sterni*, with attached soft parts.

mass at the lower end of the sternum and a persisting sinus track at the lower end of the wound. August 27, 1932, the wound was explored, with removal of a cystic mass, apparently cartilage, one centimeter in diameter. On pathologic examination, several small islands of atypical, presumably neoplastic cartilage, constituting a recurrence, were found; there was no evidence of sarcomatous change.

After the second discharge of the patient a plastic operation was successfully performed elsewhere, in order to close the persisting right empyema with bronchopleural fistula. June 20, 1939, seven and one-half years after operation, the patient reported that he was quite well and doing full-time work.

Author's Case 3.—J. R., white, male, age 47, was admitted, February 8, 1934, complaining of pain in the posterior left thorax of three months' duration, and of a tumor mass of three weeks' duration. Examination revealed a bony hard, fixed tumor the size of a small orange just to the left of the seventh dorsal spine. Roentgenographic examination (Fig. 7) demonstrated a somewhat cystic tumor arising from the head, neck, and the tubercle of the left seventh rib with pressure deformity of the adjacent ribs and of the sixth and seventh dorsal vertebrae; there were thinning and bulging of the cortex of the seventh rib. The diagnoses considered were giant cell tumor, hemangioma, osteochondroma, and osteogenic sarcoma. A biopsy specimen, taken February 10, 1934, showed it to be a chondroma. The tumor was removed February 14, 1934, by resection of the sixth to the ninth ribs posteriorly. Although the parietal pleura was readily stripped from the tumor, several tears were made in it. A part of the tumor had ap-

TABLE III

BENIGN GIANT CELL TUMOR

Author	Sex	Age	Site	Size	Initial Symptoms	Other Symptoms	Duration	Treatment	Result	Histologic Diagnosis	Remarks
(1) Fort[25]	M	11	1st rib and clavicle	—	Tumor	—	8 mos.	Excision with portions of clavicle, 1st rib and sternum (had previous operation)	Well 17 yrs. later	Benign giant cell tumor	Originally reported as sarcoma
(2) Gatewood[26]	F	14	12th rib	5x3x3 cm.	Pain	Tumor	1 yr.	Excision; radium	Well 13 yrs. later	Benign giant cell tumor	Originally reported as sarcoma
(3) Peirce[61]	M	17	10th rib	Large	Tumor	Weight loss	9 mos.	X-ray; excision with 8th to 12th ribs	Postoperative death	Chondroma osteogenic sarcoma arising in benign giant cell tumor	History of trauma
(4) Hedblom[29]	F	38	8th rib posteriorly	—	Pain	—	3 yrs.	Intercostal neurectomy for pain; resection later	Well 11 yrs. later	Benign giant cell tumor	
(5) Holland[43]	M	48	5th costochondral junction	4x3x3 cm.	Tumor	—	6 mos.	Excision	Well 11 yrs. later	Benign giant cell tumor	
(6) Neil (Samson and Haight[68])	M	9	4th rib at angle	Small	Pain	Tumor	2 mos.	Biopsy and radium	Well 11 yrs. later	Benign giant cell tumor	
(7) Samson and Haight[68]	F	31	2nd costochondral junction	3.5x2x2 cm.	Tumor	—	2 yrs.	Removal	Well 5.3 yrs. later	Benign giant cell tumor	
(8) Hilt[42]	F	15	5th rib at angle	3.5x3x3 cm.	Tumor; pain	—	6 mos.	Biopsy and x-ray	1 yr. and 10 mos later tumor smaller and calcified	Benign giant cell tumor	History of trauma
(9) Janes[46]	M	49	7th rib posterolaterally	8x5 cm. long	Pain	—	10 mos.	Removal	Died 2½ yrs. later of bronchial carcinoma	Benign giant cell tumor	

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parently invaded the vertebral bodies, and this part was not removed. The wound was closed without drainage after expansion of the lung. Convalescence was complicated by a sanguineous left pleural effusion that became purulent. Intercostal drainage was followed by open drainage, with rib resection. The patient was discharged June 8, 1934, with a narrow, draining track, which later healed.

FIG. 7.—Case 3: Postero-anterior roentgenogram of chondroma of posterior end of seventh left rib.

FIG. 8.—Case 4: Lateral roentgenogram of a very early chondroma at joint between manubrium and *gladiolus sterni*.

Pathologic examination confirmed the earlier diagnosis of chondroma growing in cancellous bone. The patient reported himself quite well, March 27, 1939, five years after operation.

Author's Case 4.—C. V., white, male, age 26, entered the hospital, November 27, 1934, complaining of a lump over the upper sternum, which had slowly increased in size since its appearance six months previously. Four months before admission, pain on pressure over the tumor had become noticeable and for three months cough and expectoration of thick sputum, tinged with blood, had been present. Twenty-six pounds had been lost during the previous two years. Examination disclosed a red, tender, firm swelling over the sternum, three centimeters below the suprasternal notch. Roentgenograms (Fig. 8) showed an irregular moth-eaten appearance of the joint between the manubrium and *gladiolus sterni* with some tumefaction external to the anterior sternal surface; sclerosis of the surrounding bone was present. There was evidence in the films of inactive, minimal, right apical pulmonary tuberculosis. November 28, 1934, the tumor was exposed and found to project seven millimeters anterior to the joint between the manubrium and gladiolus and to reach two centimeters above and below the joint. The tumor, together with the joint, was removed. No pus or other evidence of inflammation was found. Bone was removed to a depth of one centimeter from the anterior sternal surface—entirely removing the neoplastic tissue, and the wound was closed in layers, without drainage.

Histologically, the decalcified tissue of the tumor showed atypical new formation of cartilage in small nodular masses replacing bone; no defensive exudation inflammation was present, but there was new formation of connective tissue in the marrow spaces. The diagnosis was chondroma or osteochondroma, which was not sufficiently cellular to be regarded as sarcomatous. Roentgenographic study, November 15, 1935, one year

later, showed complete filling-in of the operative defect. When seen April 6, 1937, the patient presented no evidence of tumor. January 6, 1939, four years after operation, he had no signs or symptoms referable to the sternal chondroma.

Author's Case 5.—M. B., white, female, age 55, was admitted, November 3, 1937, complaining of a lump over the lower left ribs for the past year with some pain and tenderness. The mass had grown slowly for seven months before admission. Four years previously she had suffered possible fractures of the ribs in the region of the lump. A stony hard, fixed mass, was palpable in the left midaxillary line and was attached to the tenth rib. All borders were well defined except the inferior, which seemed to reach almost to the crest of the ilium. A pyelogram showed a normal position of the left kidney and roentgenograms of the thoracic wall, a somewhat loculated tumor arising from the left tenth rib in the midaxillary line without apparent invasion of adjacent ribs. The diagnosis of giant cell tumor with probable malignant change was made; osteochondroma and chondrosarcoma were also considered. The tumor was removed November 9, 1937. A diagnosis of myxochondroma was made from frozen-section examination of a portion of the tumor. The ninth, tenth, and eleventh ribs were divided at the level of the lateral border of the sacrospinalis muscle. The tumor was removed *en masse* after opening of the pleura. The peritoneum was dissected from the tumor. The patient was discharged two weeks later.

The tumor measured 10x8x8 cm.; it was surrounded by fat, and three ribs extended into it. Paraffin sections demonstrated more bone formation than had the frozen sections. A diagnosis of osteochondroma, which was somewhat invasive where it made contact with muscle, was made. The patient was reported as well, without recurrence, by her family physician, July 7, 1939, 20 months after operation.

BENIGN GIANT CELL TUMOR

Because of the rarity of benign giant cell tumor of the ribs, it seemed of interest to review all the cases adequately described in the literature. In 1935, Samson and Haight[68] presented an example from the University of Michigan Hospital. Additional follow-up information is available on this patient and is given in Table III, with data regarding six other patients from the paper of Samson and Haight, and two reported since 1935. Three cases included by Samson and Haight have been omitted because of unsatisfactory reports. Among the group listed are the instances reported originally by Fort,[25] and Gatewood[26] as sarcomata, the diagnoses having been changed by the Bone Sarcoma Registry of the American College of Surgeons to benign giant cell tumor.

Five of the benign giant cell tumors listed in Table III occurred in men, and four in women. The ages ranged from nine to 49 years. Tumor and pain were the only symptoms except for weight loss in one case with malignant change. The symptoms were of two months' to two years' duration. Two patients were treated only with radium and roentgenotherapy, respectively, with apparently good results, and are reported as living 11 years, and one year and ten months, respectively, following treatment. The remaining seven patients were treated by operative removal of the tumors with one postoperative death occurring following the removal of a chondro-osteogenic sarcoma arising in a benign giant cell tumor. A second patient died of bronchial carcinoma two and one-half years after successful removal of the benign giant cell tumor. The remaining five patients all represent "five-year cures" by

surgical treatment, and are reported living and well from 17 to five and one-third years after operation; one patient had radium therapy after removal of the tumor.

The case of Samson and Haight[68] is listed as osteitis fibrosa cystica by the Bone Sarcoma Registry of the American College of Surgeons. No reference to this disease affecting the ribs or sternum has been found in the literature.

OSTEOGENIC SARCOMA

Table IV lists 18 cases of osteogenic sarcoma of the ribs and two of the sternum, 14 occurring in men and six in women. The ages varied from 12 to 66 years. Aside from the symptoms of pain and tumor, pathologic fracture, palpitation and dyspnea, each occurred one time. The symptoms varied in duration from one week to eight years. One patient was not treated because of the presence of metastases to the regional lymph nodes and extensive local infiltration of the tumor. The neoplasms of 19 patients were removed at operation, with one postoperative death of a patient whose tumor was extensively adherent to the lung and diaphragm. Roentgenotherapy was administered in three instances following operation, once in conjunction with Coley's toxins. One patient received preoperative roentgenotherapy and Coley's toxins after the incomplete removal of an extensive chondrosarcoma. Six patients are reported dead, one postoperatively and one without treatment; one lived 11 years after the initial symptoms, before dying of his disease, six years after a second operation. Five patients are reported living with recurrent and metastatic lesions, and one additional patient, recently, has had a resection of the lower lobe of the right lung for an hematogenous metastatic tumor. Six patients are living without disease from two months to three years after treatment. Follow-up information, other than of operative recovery, is not available on two patients. No five-year cures are reported.

Some evidence bearing upon the occurrence of malignant change in benign costal neoplasms is afforded by Cabot Case No. 24212,[13] in which a costal tumor was removed four times before a metastatic pulmonary lesion became apparent. The untreated Case 8 of this article died of a massive tumor of eight years' duration, the growth of which had been slow until shortly before death; metastases to regional lymph nodes were present.

Author's Case 6.—J. B., white, male, age 34, entered the hospital December 6, 1932. Eight months previously he had fallen ten feet, striking the right side of his back and fracturing several ribs. Three months before admission he had noted a lump on the right side of the chest, accompanied by severe pain; the tumor and pain had persisted. An orange-sized mass was palpable at the level of the eighth to tenth right ribs lateral to the spine. Pathologic examination of gelatinous material aspirated from the tumor demonstrated it to be a chondrosarcoma but not sufficiently cellular to make metastasis likely. Roentgenograms showed an increase in the soft tissue shadow of the right thoracic region due to the tumor, with erosion of the eighth and ninth right transverse vertebral processes and of the vertebral portion of the right tenth rib. A number of discrete calcified lesions of the lungs were thought to be of tuberculous origin. Roentgenotherapy, with a

total dosage of 1,600 roentgen units was administered, and the patient was discharged. He was readmitted and, January 13, 1933, the tumor was found at operation to have infiltrated the sacrospinalis muscle and to have invaded the thorax to an extent that made complete removal impossible. Coley's toxins were given after this operation without benefit. He again returned to the hospital suffering with severe pain and a complete transverse myelitis, which was not relieved by laminectomy. He died September 12, 1933. Postmortem examination disclosed extensive pulmonary and epidural metastases in the region of the dorsal cord with one intradural tumor mass.

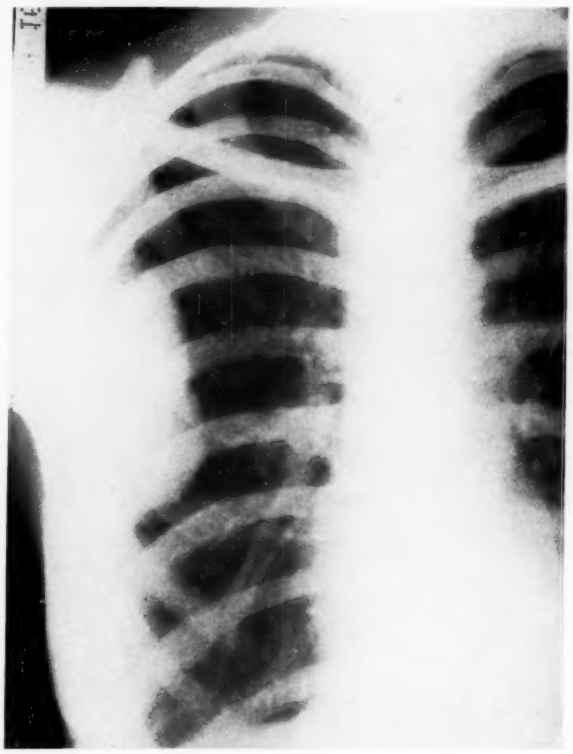

FIG. 9.—Case 7: Postero-anterior roentgenogram of chondrosarcoma of right sixth rib.

Author's Case 7.—V. W., white, female, age 24, was admitted November 30, 1937. In June, 1937, she had noted for two days sharp pain in the right axillary region and beneath the right breast, which had been aggravated by deep inspiration and movement of the right arm. During July, 1937, stiffness of the right arm was present, with cough and expectoration of foul yellow sputum. For three weeks prior to admission the patient had been aware of a swelling in the right axillary region, with a sensation of heaviness of the arm. On examination, there was felt a fixed tumor mass beneath the right posterior axillary fold; two small nodes were palpable in the right axilla and one in the left, and there was some fulness of the right supraclavicular region. Roentgenologic examination (Fig. 9) demonstrated a tumor arising from the axillary portion of the sixth rib, with irregularity in its architecture and elevation of the periosteum; secondary pressure deformity of the seventh rib was present, and the tumor extended into the chest. A diagnosis of Ewing's sarcoma was considered most likely, although osteogenic sarcoma

TABLE IV

OSTEOGENIC SARCOMA

Author	Sex	Age	Site	Size	Initial Symptoms	Other Symptoms	Duration	Treatment	Results	Histologic Diagnosis	Remarks
(1) Viannay[76]	M	29	8th, 9th and 10th ribs laterally	Nut	Tumor	—	4 yrs.	Removal with 8th to 10th ribs	Well 3 yrs. later	Chondrosarcoma	History of trauma
(2) Bigger[8]	F	12	7th rib	—	Pathologic fracture	—	—	Removal	Survived operation	Osteogenic myxofibrosarcoma	
(3) Butler[10, 11]	M	44	10th rib	—	Pain	Tumor	1 wk.	Removal	Well 3 yrs. later	Osteogenic sarcoma	
(4) Cabot Case No. 19202[12]	M	42	Several ribs (adherent to lungs and diaphragm)	Very large	Tumor	—	3½ yrs.	Partial removal	Postoperative death	Osteogenic sarcoma (chondrosarcoma)	
(5) Matson[54]	F	27	7th rib (adherent to lung)	10x7x6 cm.	Pain	Tumor	9 mos.	Removal, with 3 ribs and portion of lung; x-ray; Coley's toxins	Well 1½ yrs. later	Osteogenic sarcoma	
(6) Papin[58]	F	43	3rd, 4th, 5th ribs anteriorly	15 cm. diam.	Pain	Tumor	—	Removal, with 3rd to 5th ribs	Well 14 mos. later	Chondromyxosarcoma	Largely intrathoracic
(7) Campbell[15]	M	38	Several ribs	Large	—	Tumor, pain	2 yrs.	Partial removal	Died of metastases 3 yrs. later	Chondrosarcoma	
(8) Didier[21]	F	38	Costal cartilages	14x12 cm.	Tumor	—	2 yrs.	Removal; x-ray	Recurred 6 mos. later	Chondroosteosarcoma	Multiple cartilaginous exostoses on bones
(9) Halpert and Davis[31]	M	41	12th rib	—	—	—	—	Removal	Recurred 8 mos. later, with epidural and pulmonary metastases	Chondrosarcoma	
(10) Nissen[57]	M	32	2nd to 5th rib anteriorly	20x15x15 cm.	Tumor	Dyspnea, palpitation	1 yr.	Removal, with 4 ribs and portion of lung	Survived operation	Osteosarcoma	Extensive operation
(11) Roberg[66]	F	39	Manubrium and *gladiolus sterni*	Goose egg	Pain	Tumor	1 yr.	Removal, with division of 2nd to 5th cartilages; removal of remaining portion of manubrium 6 mos. later; x-ray after each operation	Recurred, with pulmonary metastases, 11 mos. after second operation	Chondroma, with partial transition to sarcoma	

(12) Speed[73]	M	62	2nd, 3rd, 4th ribs anteriorly	23x16x10 cm.	Tumor	—	3 yrs.	Removal, with 2nd, 3rd and 4th ribs and cartilages	Recurred in 6 mos.	Chondrosarcoma	
(13) Speed[73]	M	40	2nd, 3rd, 4th ribs anteriorly	20x16x10 cm.	Tumor	Pain	5 yrs.	Previous removal; removal with 3 ribs, portion of sternum and pericardium	Died of persistent local growth and metastases, 6 yrs. later	Chondrosarcoma	Total duration 11 yrs.
(14) Cabot Case No. 24212[13]	M	28	Left 4th rib posteriorly	Small	Tumor	—	5½ yrs.	Removal of recurrent tumor (4 previous operations in 5-yr. period)	7 mos. later metastatic tumor in rt. lower lobe of lung	Osteogenic sarcoma	Apparently began as benign chondroma. Successful removal of rt. lower lobe and portion of diaphragm for metastatic tumor
(15) Janes[16]	M	54	11th rib	Large	Tumor	—	1 wk.	Removal, with 10th and 11th ribs	Well 1 yr. later	Osteogenic sarcoma	
(16) Janes[16]	M	63	3rd rib and cartilage	7x6x5 cm.	Tumor	—	1 mo.	Removal	Extensive local recurrence 1 yr. later	Chondrosarcoma	
(17) Authors' Case 6	M	34	8th, 9th, 10th ribs posteriorly	Orange	Tumor. Pain	—	8 mos.	X-ray; partial removal; Coley's toxins	Died 7 mos. after operation of persistent tumor and metastases to spine and lungs	Chondrosarcoma	
(18) Authors' Case 7	F	23	5th, 6th ribs laterally	—	Pain	—	6 mos.	Removal with 5th, 6th, 7th ribs	Metastases to spine occurred 9 mos. later; died 25 mos. postoperatively of multiple metastases	Chondrosarcoma	X-ray therapy given after biopsy of metastatic lesion with improvement
(19) Authors' Case 8	M	66	Ribs of interscapular region	Large	Tumor	Pain	8 yrs.	Partial excision elsewhere; biopsy of metastatic lesion	Died, 2 mos. later	Myxochondroma	Bilateral axillary and local metastases present
(20) Authors' Case 9	M	49	*Gladiolus sterni*	12x6x6 cm.	Tumor	—	5 mos.	Removal with *gladiolus sterni*	Well, 2 mos. later	Chondrosarcoma	

was thought possible. A biopsy specimen of the tumor was reported as a probable sclerosing carcinoma, with scattered spherical and polyhedral cells of epithelial type. Two lymph nodes, which histologic examination showed were normal, were removed from the right supraclavicular fossa. A right pneumothorax was induced, and attachment of the lung to the tumor was seen roentgenologically. December 17, 1937, the lobulated tumor protruding between the sixth and seventh ribs was exposed. The thoracic cavity

FIG. 10.—Case 9: Chondrosarcoma of *gladiolus sterni*.

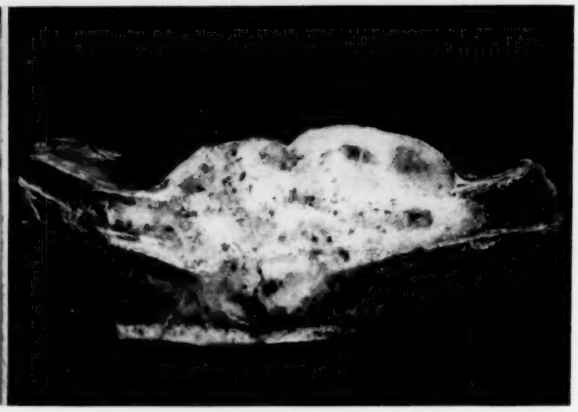

FIG. 11.—Case 9: Longitudinal section of chondrosarcoma of *gladiolus sterni* (Cf. 7).

was opened through the bed of the resected fifth rib, well above the tumor, which was removed with segments of the sixth and seventh ribs, which were divided far anterior and posterior to the neoplasm, after ligation and division of the intercostal vessels. Sharp dissection was used to free the tumor from the lung. The patient made a satisfactory recovery, and was discharged January 9, 1938.

On cross-section, the tumor was seen to be composed of a soft tissue mass, six centimeters in diameter, surrounding a rib, from which spicules of bone radiated. Microscopically, the tumor was a malignant neoplasm made up of spindle cells around foci of atypical cartilage; part of the neoplasm, a chondrosarcoma, showed hyaline fibrosis; other foci were highly cellular with hyperchromatic nuclei. The opinion was expressed that local recurrence, rather than distant metastases, was to be feared. The patient returned August 13, 1938, with a swelling at the level of the fourth dorsal spine and mild pain radiating to the right scapular region. By December 12, 1938, this mass had increased in size and a biopsy specimen showed the same histologic structure as that of the tumor originally removed. Roentgenotherapy caused complete regression of the palpable tumor. In June, 1939, a metastatic lesion in the right lung was found and treated by roentgenotherapy. Further roentgenotherapy was administered because of pain in the shoulder region. In October, 1939, the patient became paralyzed, following collapse of the first dorsal vertebra. Death from multiple widespread metastases occurred January 25, 1940, 25 months after operation.

Author's Case 8.—K. Z., white, male, age 66, was admitted December 17, 1938. He had noticed a small lump in the midline of the back eight years previously. Slow growth had taken place, until a rapid increase in size began in the Spring of 1938. The tumor was excised in September, 1938, but rapidly recurred, with an accompanying lump in the left axilla. Examination showed an irregular, firm mass five inches in diameter, fixed to the deep structures and lying across the midline, from the fourth to the tenth dorsal vertebrae. A scar, six inches long, lay across the tumor, above which was a firm, freely

movable nodule one inch in diameter. A golf-ball-sized mass was present in the left axilla and a smaller one in the right axilla. Roentgenographic examination of the thorax, in the lateral projection, demonstrated an ill-defined conglomerate mass of punctate density in the soft tissue of the posterior thoracic wall, which was thought to represent probable calcification in the tumor. The left axillary mass was removed and found, histologically, to be a myxochondroma adjacent to, and invading, a large lymph node, with wide infiltration of surrounding fat. The tumor was described as highly cellular and a recurrence with sarcomatous changes was predicted. The patient was discharged January 4, 1939, and died February 5, 1939.

Author's Case 9.—E. C., white, male, age 49, entered the hospital February 28, 1940. For five months he had noticed a progressively growing nodule located over the center of the sternum. Slight cough and ease of fatigue had been present for one month. A portion of the mass had been removed one week previously and a diagnosis of chondrosarcoma made by histologic study. Over the midportion of the sternum (Fig. 10) a firm, slightly tender mass was palpable, which was four centimeters in diameter and was elevated one centimeter above the surrounding tissue. A healing surgical scar lay over the tumor. Roentgenographic examination showed a destructive lesion involving the middle and lower portions of the sternum. Review of the pathologic sections confirmed the diagnosis of chondrosarcoma, which was more likely to recur locally after incomplete excision than to give rise to distant metastases. The patient was discharged to return after complete healing of the biopsy incision. The patient was readmitted, and, March 18, 1940, the tumor and sternum were removed. The third to the seventh left and the right costal cartilages were divided lateral to the tumor and the sternum was transected just below the manubrium. The tumor was carefully freed by blunt dissection from the pleurae and from the prepericardial fat. A small tear in the left pleura was left open to provide for drainage of wound serum into the left pleural cavity, so as to avoid cardiac tamponade. The wound was closed by mobilization and suturing together of the pectoralis major muscles in the midline, and by closure of the skin without external drainage. On the second day following operation intratracheal and intrabronchial catheter suction was employed to remove bronchial secretions. Further convalescence was uneventful. The patient was discharged April 20, 1940.

Pathologic examination of the tumor (Fig. 11) again confirmed the diagnosis of chondrosarcoma. A marked similarity of the specimen to that of Case 2 (Fig. 7) was noted. The roentgenographic appearance of the two neoplasms was also quite similar. The patient was well, May 21, 1940, two months after operation.

EWING'S SARCOMA

Table V lists data regarding 18 patients suffering with Ewing's sarcoma, apparently primary in ribs. In an effort to list all available cases of Ewing's sarcoma, primary in the bony thoracic wall, in the literature, the cases of Hedblom,[38, 39] and Harrington,[34] reported as sarcoma and endothelioma, respectively, have been included since, from the published descriptions, the tumors were in all likelihood examples of this neoplasm. In addition, the case of Reeves and Kassabach,[65] included by Hedblom,[39] and two of Geschickter and Copeland,[27] omitted by Hedblom,[39] have been listed. In reviewing the cases collected by Hedblom,[39] five probable instances of Ewing's sarcoma were found in the reports of Key,[50] Juge, de Vernejoul, and Astier,[49] Denk,[19] Polloson and Novel,[63] and Harrington;[34] these cases are not listed in Table V, since the evidence is not positive that they represented Ewing's sarcoma.

TABLE V

EWING'S SARCOMA

Author	Sex	Age	Site	Size	Initial Symptoms	Other Symptoms	Duration	Treatment	Results	Histologic Diagnosis	Remarks
(1) Hedblom[38, 39]	M	15	4th rib anteriorly and laterally	12x6x4 cm.	Pain	Tumor	9 mos.	Removal, with 3rd, 4th, 5th ribs; x-ray	Died 5 mos. later of recurrence	Sarcoma	Photomicrograph, and course typical of Ewing's sarcoma
(2) Harrington[33]	F	15	4th to 8th ribs posteriorly	Large	Pain	Tumor	5 mos.	Partial removal, with 4th to 8th ribs; radium	Death 3 mos. later of pulmonary and spinal metastases	Endothelioma	
(3) Reeves and Kassabach[65]	F	18	9th rib posteriorly	8x5x5 cm.	Pain	Pleurisy	3 mos.	Partial removal, with 8th, 9th, 10th ribs; x-ray; Coley's toxins	Death 10 mos. after operation, with metastases to lung, pleura and liver	Sarcoma, probably Ewing's	
(4) Geschickter and Copeland[27]	F	15	4th rib	—	—	Tumor; pain	18 mos.	Removal; second removal 18 mos. later	Died few mos. later	Ewing's sarcoma	
(5) Geschickter and Copeland[27]	M	27	Ribs	—	Dyspnea	Tumor	3 mos.	Radiation	Died	Ewing's sarcoma	
(6) Tavernier[75]	M	12	11th, 12th ribs. 11th and 12th thoracic, 1st lumbar vertebrae	Large	Pain	Tumor and paraplegia	6 mos.	Biopsy and x-ray	Tumor not palpable but paralysis continued; died 6 mos. later	Ewing's sarcoma	
(7) Campbell[14]	F	10	Rib	—	—	—	4 mos.	X-ray	Well, 2 mos. later	Ewing's sarcoma	
(8) Dagneau, Pichette, and Morin[18]	M	16	11th rib	10x6 cm.	Tumor	Pain	3 mos.	Removal, with 11th and 12th ribs; x-ray (had two previous operations)	Recurrence and metastasis to lungs and skull; death after treatment of metastases	Ewing's sarcoma	Earliest diagnosis of infection
(9) Herbert[40]	M	10	6th rib, laterally	—	Pain	Fever; pleural effusion	3 mos.	Removal; x-ray	Died, 1 mo. later	Ewing's sarcoma	

(10) Herbert[10]	M	20	3rd rib, laterally	Large	Pain and tumor	Loss of weight	3 mos.	Biopsy; x-ray	Died, very shortly	Ewing's sarcoma	Intrathoracic extension and pulmonary metastases present at time of diagnosis
(11) Bergstrand[6,7]	M	15	5th and 6th ribs, posterolaterally	500 Gm.	Pain	Tumor	15 days	Removal; x-ray for metastases later	Pulmonary metastases, 2½ and 5 yrs. later, which regressed with treatment; died of metastases, 6 yrs. after operation	Ewing's sarcoma	Excellent response to first roentgenotherapy
(12) Bergstrand[6]	M	10	6th, 7th ribs, laterally	—	Malaise	Tumor; pain	6 mos.	Removal, probably incomplete	Living, 1½ yrs. later, with pulmonary and osseous metastases		
(13) Bergstrand[6]	M	10	6th, 7th ribs, laterally	8x5 cm.	Tumor	Pain	1 mo.	X-ray; removal, with 6th and 7th ribs	Survived operation	Ewing's sarcoma	
(14)Bergstrand[6]	M	14	8th rib, posteriorly	Right thorax filled	Pain	Tumor and dyspnea	12 mos.	X-ray	Immediate improvement	Ewing's sarcoma	
(15) Geschickter and Copeland[28]	M	22	Rib	—	Pain	—	12 mos.	Curettage	Died, 3 yrs. later	Ewing's sarcoma	
(16) Geschickter and Copeland[28]	M	30	Rib	—	Cough; pleurisy	—	6 mos.	X-ray	Died, 2 yrs. later	Ewing's sarcoma	
(17) Geschickter and Copeland[28]	M	11	Rib	—	Pain	Pleural effusion	3 mos.	X-ray	Died, 3 mos. later	Ewing's sarcoma	History of trauma
(18) Authors' Case 10	F	22	11th rib, posteriorly	9x8x6 cm.	Pain	Tumor	2 mos.	Biopsy; x-ray	Died, 7 mos. later	Ewing's sarcoma	8 mos. pregnant at onset; uneventful delivery

The symptoms of the listed cases of Ewing's sarcoma of the ribs are tumor and pain with the addition of dyspnea, pleurisy, and pleural effusion, each two times; and fever, malaise, loss of weight, cough and paraplegia from metastases, each once. Thirteen patients were men, and five were women, whose ages varied from 10 to 30 years. In no case had symptoms been present for more than one year before treatment. The tumors were treated by operation alone in four instances, and by operation combined with irradiation in six instances; Coley's toxins were administered to one of the latter group of patients. Irradiation alone was the treatment administered to eight patients. There were no deaths due to operation.

The results of treatment of Ewing's sarcoma of the ribs were poor. Fourteen of the 18 patients are reported dead of their disease, ten dying 13, or fewer months after treatment; and three, two, three, and six years, respectively, after treatment. The duration of life before death of one patient is not stated. One patient is reported living with disease and one-half years after treatment, and another as living and well two months after treatment. Follow-up data are not given regarding two patients. The best therapeutic result is that already described in the patient reported by Bergstrand;[6, 7] this boy, age 15, lived six years after removal of the apparently primary costal tumor, and on two occasions very extensive pulmonary metastases disappeared following roentgenotherapy. While successful surgical removal would certainly be possible, should a case be diagnosed and treated before metastases have occurred, it seems likely that roentgenotherapy will be the chief reliance in treatment of Ewing's sarcoma of the ribs. In many instances extensive tumors were present among the listed cases, often with metastases characteristically involving other bones, the lungs, and pleura. Earlier diagnosis should, occasionally, be made if Ewing's sarcoma is borne in mind during the examination of patients complaining of costal pain without apparent cause and with or without palpable tumor. The neoplasm invariably occurs in persons younger than 30 years of age.

Author's Case 10.—L. H., white, female, age 22, was admitted, July 16, 1937, complaining of a tumor in the left thoracic region of two and one-half months' duration, that had been called to her attention by severe pain. The tumor had grown steadily. One month before admission she had been delivered of a normal child at term. The patient appeared chronically ill. Just behind the posterior axillary line, overlying and fixed to the tenth, eleventh, and twelfth left ribs was a firm, slightly lobulated, not tender undiscolored mass measuring 9x8 cm. No bruit or thrill was present. Roentgenologic examination demonstrated destruction of a portion of the tenth rib and elevation and paralysis of the hemidiaphragm. No Bence-Jones protein was present in the urine, although albumen was.

Examination of the blood disclosed 55 per cent hemoglobin (9.4 Gm.); 4,290,000 red blood cells; 8,100 white blood cells, with 54 per cent polymorphonuclear neutrophils, 21 per cent large lymphocytes, 4 per cent small lymphocytes, 11 per cent monocytes, and 11 per cent eosinophils, with plasma cells present, and platelets in normal quantities. One per cent of the red blood cells were reticulocytes. Dr. Raphael Isaacs, who examined the patient and the blood stated: "A hypochromic, hyperplastic type of anemia is present suggestive of a chronic nephropathy. Marked eosinophilia is present. Thrombosis should

be expected if operative procedures are used. While the plasma cells are suggestive of a myeloma, hypernephroma should be considered in the differential diagnosis."

Pathologic examination of a specimen from the tumor secured by punch biopsy, demonstrated a round cell sarcoma without evidence of bone formation, which was probably an endothelial myeloma (Ewing's sarcoma) but which might have been a primitive myeloblastoma. Roentgenotherapy was begun and the patient was discharged, the therapy being continued at home. She died shortly afterwards of widespread metastases.

FIBROSARCOMA

Six instances of fibrosarcoma involving ribs are listed in Table VI. The neoplasm probably did not in any case originate in the bones, although it was intimately associated with them at the time of treatment; this sequence is clearly illustrated by Case 12 of this report. Three men and three women from 34 to 61 years of age were affected. The symptoms of the large tumors were of from four months' to four and one-half years' duration. Two patients were treated with roentgenotherapy and the remaining four were treated by operation, with one postoperative death. From this small group of cases the results of therapy are not encouraging, since four patients are dead, one is living with metastatic lesions, and information after operative recovery is not available about one patient.

Author's Case 11.—E. P., white, female, age 46, was admitted June 17, 1932. For two years a sensation of heaviness had been present in the posterior, left thoracic region. Since the patient had struck the left chest two months before admission, sharp pain radiating anteriorly was felt. She had noticed a lump, which had reached orange-size, over the left chest posteriorly for one month. The debilitated patient was extremely uncomfortable, and a tender fist-sized tumor was palpable in the region of the left seventh, eighth, and ninth ribs posteriorly. Enlarged lymph nodes were palpable in both axillae and above the left clavicle. Roentgenographic examination demonstrated a soft tissue mass lying over the posterolateral portion of the left thorax, with destruction of segments of the seventh and ninth ribs and erosion of the eighth rib. Pathologic examination of a portion of the tumor removed showed it to be a large cell fibrosarcoma with extensive necrosis. Roentgenotherapy was ineffective in controlling the pain caused by the tumor, which increased in size. The patient was discharged and died in September, 1932, two months later.

Author's Case 12.—J. P., white, female, age 50, was admitted March 21, 1935. Four months previously she had become aware of tightness about the right scapula, especially when abducting the arm. During the four weeks prior to admission a mass, which had grown rapidly, was present near the right scapula. On examination, a rubbery, tender tumor, fixed to the deep structures, was palpable between the right scapula and the spinal column; it extended the entire length of the scapula. Roentgenographic study showed a soft tissue tumor over the right chest posteriorly with pressure atrophy or invasion of ribs, especially the third, fourth, and sixth. Right pneumothorax was induced April 8, 1935. Roentgenograms then demonstrated that the tumor extended into the thoracic cavity. The tumor, which was regarded as a neurofibroma, lipoma, or sarcoma, was exposed through a thoracoplasty incision April 12, 1935. Frozen-section examination, of a portion removed, showed the neoplasm to be a fibrosarcoma. The tumor was removed by division and resection of portions of the second to the eighth ribs and removal of the corresponding vertebral spinous and transverse processes with portions of the laminae. The sacrospinalis muscle had been invaded but not the pleura, which was opened widely. The patient died on the fifth postoperative day. Necropsy demonstrated that death was due to bilateral pulmonary atelectasis.

TABLE VI

FIBROSARCOMA

Author	Sex	Age	Site	Size	Initial Symptoms	Other Symptoms	Duration	Treatment	Result	Histologic Diagnosis	Remarks
(1) Takabatake[74]	M	61	3rd rib, anteriorly	Head	Tumor	—	1 yr.	Removal, with 2nd, 3rd, 4th ribs	Died a few mos. later	Fibrosarcoma	
(2) Takabatake[74]	M	41	8th, 9th ribs, laterally	Large	Tumor; pain	—	6 mos.	Biopsy; x-ray	Living, 10 mos. later	Fibrosarcoma	Metastases to lungs and lymph nodes present
(3) Speed[72]	F	34	Axillary portion of thoracic wall	Grapefruit	Tumor	—	2 yrs.	Removal; Removal, with 4 ribs	Death, 1 yr; after 2nd operation of pulmonary metastases	Fibrosarcoma	Recurred 6 mos. after 1st operation
(4) Cohn[16]	M	42	1st, 2nd ribs, anteriorly	Large	Tumor	Pain	4½ yrs.	Removal, with clavicle and 1st, 2nd ribs (previous operation and x-ray therapy)	Survived operation	Fibrosarcoma	History of trauma
(5) Authors' Case 11	F	46	7th, 8th, 9th ribs, posteriorly	Orange	Pain	Tumor	2 yrs.	Biopsy; x-ray	Death, 2 mos. later	Fibrosarcoma	Tumor inoperable
(6) Authors' Case 12	F	50	Interscapular region	12x6x6 cm.	Pain	Tumor	4 mos.	Removal, with 2nd to 8th ribs	Postoperative death	Fibrosarcoma	Ribs not actually invaded but surrounded by tumor

Pathologic examination showed the tumor, which passed between the ribs and was closely adherent to them and infiltrated the costal periosteum, to be a spindle cell fibrosarcoma with moderate differentiation.

UNCLASSIFIED SARCOMA

Table VII lists data concerning five patients suffering with tumors described as round cell sarcomata, four involving the ribs and one the sternum. Three patients were men, and two women. The ages varied from four to 29 years. Tumor and pain were the only symptoms. One very large tumor of the sternum was merely biopsied, and the four neoplasms of the ribs were resected, with one death due to operation. The most interesting case is that of Hautefort,[36] in which the middle lobe of the right lung, adherent to the tumor, was successfully removed, with the tumor and three ribs, from a four-year-old child. No adequate follow-up information is available about these patients other than on the one dying postoperatively.

HODGKIN'S DISEASE AND LYMPHOSARCOMA

Data are given, in Table VIII, regarding four patients with Hodgkin's disease of the sternum and ribs, and two with lymphosarcoma of the ribs. The sex of one patient is not stated, and three were men, and two women. The ages varied from 9 to 39 years. The duration of symptoms of four cases was relatively long—from three to six years; the duration of symptoms of two cases was six months and one and one-half years. Three patients were treated with roentgenotherapy alone; one had an extensive resection of the anterior thoracic wall some time after radiation therapy, one had a limited removal of the involved bones with later roentgenotherapy, and the sixth was treated with excision alone. Three patients with Hodgkin's disease are reported living six, 16 and 18 months, respectively, after treatment, one each with Hodgkin's disease and lymphosarcoma are dead, and one with lymphosarcoma is reported as surviving operation.

In all likelihood the great majority of tumors of the lymphoblastoma group involve the bony thoracic wall secondarily. The close anatomic relationship of the mediastinum to the anterior thoracic wall explains invasion of the sternum and anterior ribs by Hodgkin's disease of the mediastinum. Harrington, Dorsey, and Strohl[35] described a Hodgkin's tumor presenting through an intercostal space on the anterior thoracic wall without rib involvement.

Author's Case 13.—F. D., white, female, age 28, was admitted March 29, 1934. In September, 1932, 19 months previously, a bulging of the anterior thoracic wall accompanied by dull pain had appeared. After roentgenologic study the mass was incised in July, 1933. Tubercle bacilli could not be demonstrated in the caseous material removed at this time. A therapeutic abortion was performed in October, 1933, because of suspected pulmonary tuberculosis. Several hemoptyses occurred in the months just prior to admission. Examination disclosed a firm orange-sized mass fixed to the sternum at the level of the second and third ribs. A surgical scar ran over the center of the mass, and thin seropurulent material drained from a sinus at its base. Roentgenologic study of the lungs and thoracic wall, in the postero-anterior, oblique, and lateral projections, demonstrated an infiltrating lesion of the anterior portion of the upper lobe of the left

TABLE VII

UNCLASSIFIED SARCOMA

Author	Sex	Age	Site	Size	Initial Symptoms	Other Symptoms	Duration	Treatment	Results	Histologic Diagnosis	Remarks
)Vitale[77]	M	19	Sternum	Very large	Pain	Tumor	4 yrs.	Biopsy	No follow-up	Small round cell sarcoma	
(2) Vitale[77]	M	23	12th rib	6x3 cm.	Tumor	—	3 mos.	Removal, with 12th rib and soft tissue	Recurred in 2 mos.; and removed again	Round cell sarcoma	
(3) Vitale[77]	F	29	12th rib	Orange	Tumor	—	6 mos.	Removal, with 12th rib	Postoperative death	Small round cell sarcoma	
(4) Hautefort[36]	M	4	3rd, 4th, 5th ribs anteriorly	10 cm. diam.	Tumor	—	4 mos.	Removal, with 3rd, 4th, 5th ribs and middle lobe of right lung	Survived operation	Round cell sarcoma of connective tissue origin	Middle lobe of lung adherent to, but not invaded by tumor
(5) Martin, Henry and Soustelle[53]	F	26	10th rib; posteriorly	—	Pain	Tumor	More than 1 yr.	Removal, with 10th rib	Survived operation	Round cell sarcoma	

TABLE VIII

HODGKIN'S DISEASE

Author	Sex	Age	Site	Size	Initial Symptoms	Other Symptoms	Duration	Treatment	Results	Histologic Diagnosis	Remarks
(1) FontsAbreu[24]	F	39	Sternum	6x3 cm.	Tumor	—	3 yrs.	Biopsy; x-ray	Well, 16 mos. later	Hodgkin's disease	
(2) Behrend[5]	—	13	1st, 2nd ribs, with cartilages, sternum and clavicle involved	10x8x3 cm.	Tumor	—	5 yrs.	Previous x-ray; resection with 1st and 2nd ribs; x-ray	Well, 1½ yrs. later (3 yrs. from 1st treatment)	Hodgkin's disease	Little mediastinal disease before operation
(3) Paraf, Fischgold, Abaza, and Lewi[59]	M	26	Manubrium sterni	Moderate	Pain	Tumor	6 mos.	Biopsy; x-ray	Axillary nodes and skin involved, 5 mos. later	Hodgkin's disease	
(4) Authors' Case 13	F	28	Sternum; 2nd, 3rd costal cartilages	Large	Tumor; pain	—	18 mos.	Previous incision; partial excision; x-ray	Died, 2 yrs. later	Hodgkin's disease	Appearance of associated pulmonary lesion in x-ray, suggestive of pulmonary tuberculosis
LYMPHOSARCOMA											
(1) Lowenberg and Ginsberg[52]	M	9	10th rib	Large	Pain	Tumor	5 yrs.	Biopsy; x-ray	Death, 6 mos. later	Lymphosarcoma	Received serum therapy for hopeless malignancy, experimentally
(2) Brun and Cursieres[9]	M	26	9th, 10th, 11th ribs	20x16x11 cm.	Pain	Tumor	6 yrs.	Excision, with 9th, 10th and 11th ribs	Survived operation	Lymphosarcoma	

TABLE IX

MISCELLANEOUS TUMORS

Author	Sex	Age	Site	Size	Initial Symptoms	Other Symptoms	Duration	Treatment	Results	Histologic Diagnosis
(1) Ivanissevich, Egues and Fernandez[41]	M	17	9th rib, posteriorly	7x5x5 cm.	Pain	—	7 mos.	Excision	Survived operation	Schwannoma
(2) Authors' Case 14	M	27	10th rib, posteriorly	—	Pain	—	Some mos.	Removal	Well, 34 mos. later	Fibroma
(3) Authors' Case 15	F	30	5th rib, laterally	5x5x2½ cm.	Pain	—	4 yrs.	Removal, with 4th and 5th ribs; periosteum of 6th rib	Well, without recurrence, 28 mos. later	Neurofibroma

lung with central excavation, which was considered tuberculous. Gross destruction of the manubrium and upper *gladiolus sterni* was present, with involvement of the left second and third costal cartilages. Tubercle bacilli could not be found in smears made from the fluid draining from the sinus. Nevertheless, a diagnosis of tuberculosis of the thoracic wall was made. The tumor mass was, in part, excised and found to be composed of a hard shell of tissue covering a caseous mass that extended into the mediastinum and lung.

The histologic diagnosis of Hodgkin's disease was later confirmed by examination of a lymph node removed from the left axilla. A considerable clinical and roentgenologic improvement followed the administration of 800 units of roentgenotherapy. The improvement continued when the patient was last seen, September 25, 1934, five months after treatment. She died, elsewhere, May 12, 1936, two years after roentgenotherapy.

MISCELLANEOUS NEOPLASMS

Table IX lists data relative to three patients suffering from a fibroma, a schwannoma, and a neurofibroma, respectively. The fibroma was a primary costal tumor, while the schwannoma and neurofibroma were in close relationship to ribs. Case 15 of this report illustrates the close association of a benign tumor of nerve sheath origin to the ribs, which required the resection of two ribs and the periosteum of another with the tumor. The pathogenesis of schwannoma and neurofibroma will not be discussed here. All three patients were treated by operation. The two with fibroma and neurofibroma are living and well 34 and 28 months, respectively, after operation and the one with schwannoma is reported merely as surviving operation.

Author's Case 14.—A. A., white, male, age 27, was admitted, December 21, 1932, complaining of pain in the back and knees of some months' duration. Roentgenograms of the spine, which confirmed the clinical diagnosis of arthritis, revealed also a tumor of the posterior portion of the left tenth rib. Further roentgenographic study (Fig. 12) demonstrated the homogeneous, expansile tumor covered by a thin shell of calcified tissue. The tumor, which had not broken through its bony cortex, was removed with the adjacent portions of the left tenth rib, January 9, 1933. The pleura was not opened. The patient was discharged some time later after treatment of the arthritis.

The pathologic diagnosis was a very cellular fibroma approaching a spindle cell sarcoma. November 23, 1935, 34 months after operation, the patient was well, without recurrence of the tumor.

Author's Case 15.—V. W., white, female, age 30, was admitted February 4, 1938. A roentgenographic examination (Fig. 13), December 10, 1937, had been made because of discomfort in the chest and had revealed a circumscribed mass in contact with the fourth to sixth ribs in the right posterior axillary line. Two and one-half years previously, the patient had had an attack of pleurisy with effusion. No change in the mass, which was associated with slight irregularity of the fourth rib, was noted in another study one month later. Physical examination of the patient found no evidence of a thoracic wall tumor. The diagnoses considered were tuberculous abscess, pulmonary tuberculosis, and primary or metastatic tumor. February 3, 1938, the tumor, together with the adjoining segments of the fourth and fifth ribs and the periosteum of the sixth rib, was removed. The tumor, which extended beneath the sixth rib, was dissected bluntly from the lung. Aspiration before section of the ribs had demonstrated the mass to be solid. The patient was discharged 11 days after operation.

The specimen consisted of portions of two ribs seven and one-half and nine centi-

meters long, respectively, with an encapsulated tumor, 5x3 cm., firmly attached to one rib. Microscopic examination showed the tumor to be a neurofibroma, probably arising from an intercostal nerve, although this could not be definitely demonstrated; the ribs were not involved. The patient was quite well in May, 1940, 28 months after operation.

METASTATIC TUMORS

During the study of the hospital records many instances of malignant tumors, metastatic to the ribs, were found. The sites of primary origin were

FIG. 12.—Case 14: Postero-anterior roentgenogram of fibroma of left tenth rib.

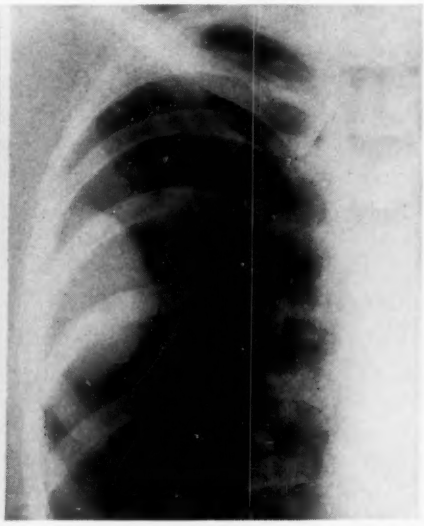

FIG. 13.—Case 15: Postero-anterior roentgenogram of neurofibroma, closely adherent to the right fourth, fifth, and sixth ribs.

in many different organs. In several cases the metastatic costal tumors were the presenting lesions. Crile[17] has discussed pulsating tumors of the sternum, metastatic from carcinomata of the thyroid and kidney. Roth and Davidson[67] have reported an additional case of pulsating sternal tumor secondary to an hypernephroma.

SUMMARY

Data have been presented regarding 66 cases of neoplasms of the bony thoracic wall, collected from the literature since 1933, and 15 cases from the University of Michigan Hospital; the collected cases include two of Ewing's sarcoma reported by Geschickter and Copeland,[27] in 1931, and not included in Hedblom's[39] 1933-report. In considering benign giant cell tumor and Ewing's sarcoma, an effort has been made to gather all known cases from the literature; four and three cases, respectively, were reported prior to 1933, in addition to the two mentioned. These seven cases were included by Hedblom.[39]

The treatment of the great majority of tumors of the bony thoracic wall

has been by operation, at which an effort was usually made to remove the neoplasm completely. In some instances several operations were performed. Twenty-seven cases of benign tumors (osteomata, chondromata, benign giant cell tumors, fibroma, schwannoma, and neurofibroma) reported since 1933, were treated surgically, with one death due to operation (3.7 per cent). Thirty-six malignant tumors (osteogenic sarcomata, Ewing's sarcoma, fibrosarcoma, unclassified round cell sarcomata, Hodgkin's disease, and lymphosarcoma) reported since 1933, were treated by operation with three deaths due to operation (8.5 per cent). Radiation therapy was employed in conjunction with surgery in a number of instances. Fourteen patients (seven of them with Ewing's sarcoma) were treated with radiation alone, and two patients received no treatment whatever.

Although extensive follow-up information is, unfortunately, not available for any group of cases except those of benign giant cell tumor, some conclusions as to the results of therapy may be drawn: The greatest therapeutic success has been obtained in benign giant cell tumor, with five cures of more than ten years' duration, and one of more than five; four of the cures of long duration are in patients reported prior to 1933. Among the patients with chondromata, there are three five-year cures, and three patients are living and well more than two years after operation. One patient, who was operated upon for an osteoma, is living and well, two years later; and patients with a fibroma and a neurofibroma are well 34 and 28 months, respectively, after operation. The striking fact about the 33 patients with benign tumors is that only three are reported as dead.

Among the malignant tumor groups there is no case with a five-year cure, and only two of osteogenic sarcomata with three-year cures. The most discouraging group from the standpoint of therapy, is that of Ewing's sarcoma, with 14 of 18 patients reported dead, and one reported living with recurrence; adequate follow-up information is not available relative to the other three patients. Of the 20 patients with osteogenic sarcoma, six are reported as dead, and five as living, with recurrent and metastatic tumors. Four of the six patients with fibrosarcoma are reported as dead, and a fifth as living, with metastases.

Long periods of follow-up are not given for the five patients with unclassified sarcomata, and the six patients with tumors of the lymphoblastoma group, although one and two, respectively, are known to be dead. There is a marked difference in the results obtained from treatment of the benign and malignant groups of tumors affecting the ribs and sternum. Twenty-seven of the 55 patients with malignant tumors are known to be dead.

Complete surgical removal of tumors of the ribs and sternum appears to be the most effective form of therapy. The mortality of surgical treatment of these tumors has been low in recent years. Very extensive operations have been carried out successfully to remove huge tumors, even those directly involving the lung. Roentgenotherapy has been ineffective, except in two cases

of benign giant cell tumor and, palliatively, in one case of metastatic Ewing's sarcoma.

The authors acknowledge, with appreciation, the follow-up information regarding patients given to them by Professor Hilding Bergstrand and Dr. Ethan Flagg Butler.

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AUTOPLASTIC TRANSPLANTATION OF SPLENIC TISSUE, IN MAN, FOLLOWING TRAUMATIC RUPTURE OF THE SPLEEN

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AT THE HILLMAN HOSPITAL, Birmingham, Ala., during a seven-year period, from 1933 through 1939, there were 457 cases with acute abdominal injury, including penetrating wounds, as well as subcutaneous injury, admitted to the hospital. Among these cases, only 17, or 3.7 per cent, of the whole number, were instances of traumatic rupture of the spleen. According to Berger,[3] about 51 per cent of individuals who experience acute rupture of the spleen, die of hemorrhage within one hour of the accident. Of those that survive this primary mortality, 15 to 55 per cent will die within a few days, in spite of the best modern surgical treatment for acute traumatic rupture of the spleen. Besides this, there is a huge fatality rate of 90 to 100 per cent, for individuals suffering such an accident, who refuse, or do not receive surgical intervention. Consequently, human survivals of traumatic rupture of the spleen are, indeed, small in number. The chances of a person in this group of survivals, either having an abdominal surgical exploration, or coming to autopsy examination at some future date, would be proportionally much less; which may account for the rare disclosure of the condition which was found upon postmortem examination of the abdomen, in the case to be described. The numerous spleen-like nodules found scattered over the peritoneum, including the surfaces of the omentum, small and large bowel, the diaphragm, and the pelvic cavity, were not accessory spleens, but small splenic implants. These implants grew from viable splenic pulp cells dispersed over the peritoneal cavity, as a result of the intra-abdominal splenic hemorrhage, when this normally vascular organ ruptured. Some of these viable cells, normally situated in the splenic parenchyma, were torn away by the force of the trauma and bleeding, to float with the hemorrhage to a new location, and graft themselves diffusely on living peritoneum. With the passage of time, a fibrous reaction, or capsule, formed about these nests of splenic cells, as they underwent division and growth, in their new beds. Parenchymatous cells of no other abdominal organ are known to exhibit similar characteristics; excepting, possibly, the uterine endometrium.

Case Report.—Hosp. No. 101843: H. M., colored, male, age 9, entered Division A, Surgical Service, Hillman Hospital, September 30, 1935, about five and one-half hours after he had fallen out of a tree, striking his abdomen on the ground. Abdominal pain

was immediately complained of, mainly in the region of the umbilicus. He had not become unconscious, nor had he vomited. There had been no gross hematuria.

Physical Examination.—Temperature, per rectum, 100.6° F.: pulse, 152; blood pressure 90/54. The patient appeared apprehensive; with tense nares; and rapid, shallow respirations. Lungs were negative. The abdomen was moderately distended, and rigid. There was general abdominal tenderness on palpation, which was more marked in the left upper abdominal quadrant, and left flank. An increase in flank dulness was noted, which seemed to shift.

Hemoglobin 50%; R.B.C. 3,010,000; W.B.C. 15,500, with 89% neutrophils, and 11% lymphocytes. Uranalysis: 150 mg. albumin, microscopically, a few glanular casts, together with four to six leukocytes, and 50 to 60 red blood cells per high power field. One hour later, the hemoglobin was 49%, R.B.C. 3,000,000. The pulse becoming more rapid. *Clinical Impression:* Ruptured abdominal viscus; exploratory celiotomy advised. Before operation 1,000 cc. of normal saline was administered by hypodermoclysis.

Operation.—R. A. H.: Two and one-half hours after admission: Under ether anesthesia, the abdomen was opened through an upper left rectus incision. A large amount of free blood was found present, and the spleen was found to be ruptured, almost in half, with active bleeding. A splenectomy was rapidly performed. No spleen-like nodules were noted within the abdomen. During operation intravenous gum acacia solution was administered, and this was immediately followed by a blood transfusion.

TABLE I

SERIAL BLOOD COUNTS*

Date	Hemoglobin	Red Blood Cells	Color Index	Leukocytes	Neutrophils	Lymphocytes	Large Mononuclears	Eosinophils	Basopnils	Time Relation to Operation
9/30/35	50%	3,010,000	0.8	15,500	89%	11%				On entrance. Preoperative
9/30/35	49%	3,000,000	0.8							1 hour later
10/ 1/35	45%	2,720,000	0.8	12,950	86%	14%				1st day, P. O. After blood transfusion
10/ 7/35	37%	2,530,000	0.7							P. O. 7th day
10/10/35	40%	2,150,000	0.9							P. O. 10th day
10/14/35	65%	3,560,000	0.9	14,050	82%	12%	3%			P. O. 14th day. After blood transfusion
10/17/35	47%	2,460,000	0.9	6,350	55%	43%		2%		P. O. 17th day

* In the case reported. These were taken during the patient's first stay in the hospital, as a result of the acute traumatic rupture of the spleen.

Except for some abdominal distention during the early postoperative phase, which was combated with a stomach tube, and the presence of a secondary anemia, the convalescence was essentially uneventful. The wound healed per primam; and the dressing was removed 13 days after operation.

Second Admission.—Thirty-nine months later, on January 1, 1939, when the boy was age 13, he was again admitted to the Hillman Hospital, on the Medical Service, Hosp. No. 127278, with a clinical diagnosis of acute tetanus, contracted from an injury of his left little finger by the explosion of a firecracker on December 25, 1938, six days previously. In spite of energetic treatment with tetanus antitoxin, the patient died 20 hours after he entered the hospital. An autopsy (Dr. J. D. Bush) was performed two and one-half hours after death. Only a portion of the complete autopsy report will be included.

Postmortem Examination.—(A-39-2): The changes of greatest interest were limited to the thoracic and peritoneal cavities. The upper anterior mediastinum was filled by a bilobed thymus gland, which weighed 61 Gm. The tracheobronchial lymph nodes were large and contained black pigment. There were several fibrous adhesions binding the healed splenectomy wound to various loops of bowel and to the omentum. There were numerous adhesions about the splenic bed and one spleen which measured 3 by 4 cm. was firmly adherent to the splenic bed. Scattered over the abdomen were several dozen firm, dark red nodules which measured from 0.5 to 1 cm. in diameter. These were found on the inferior surface of the left dome of the diaphragm, the omentum, the small bowel, the ascending colon, the transverse colon, the descending colon and over the pelvis including the anterior surface of the rectum and the rectovesical pouch. The smaller ones were rounded; the larger ones were flat and measured 0.2 to 0.3 cm. in thickness. All were sessile and covered with serosa. In color and consistency they closely resembled splenic tissue. The surface was red and on section there was a thin, white fibrous capsule enclosing a firm, dark red, spleen-like tissue. The total number of the nodules was approximately 75.

Pathologic Examination.—Microscopic:—Sections of the nodules revealed a structure morphologically similar to adult spleen. Each nodule was surrounded by a capsule composed of fibrocytes and collagenous fibers. The convex surface of the capsule was covered by a layer of flattened endothelial cells continuous with the serosa of the structures to which the implant was attached. In the capsule there were scattered foci of lymphocytes, particles of iron pigment and small blood vessels filled with erythrocytes. Trabeculae extended from the capsule into the pulp, occasionally traversing the entire width of the nodule. These trabeculae possessed a structure similar to the capsule and were accompanied by small blood vessels. There were a number of follicles present, each composed of lymphocytes; in a few an arteriole was also present. No germinal centers were evident. The red pulp was composed of sinuses lined by a single layer of cells with prominent nuclei. The sinuses were filled with erythrocytes, polymorphonuclear, neutrophils and a few endothelial leukocytes. An occasional siderophage was seen in the red pulp.

Discussion.—In medical literature, there apparently have been only ten similar cases described. Two other autopsy examinations were reported, in which spleen-like nodules were so diffusely scattered over the abdominal cavity, as to practically rule out their author's diagnosis of accessory spleens. These two last mentioned autopsy examinations were made on individuals who gave no history of trauma, and had not undergone a splenectomy. However, in both instances the spleen and surrounding area presented gross findings, usually associated with residuals from healed trauma. Consequently, one might well reason that these cases represented splenic implants from traumatic splenic ruptures which had healed, and will be so considered. Table II briefly summarizes the 12 cases described in the literature, as well as our own case. Only three such cases have been reported in American medical literature, and these were published since September, 1939; two of these were by the same author. A detailed review of the earlier reported cases is made in the excellent articles by Shaw and Shafi; Jarcho and Anderson; and Buchbinder and Lipkoff. Buchbinder and Lipkoff recognize Foltin, who described a case in 1911, as being the first to suggest that the spleen-like nodules in question, were splenic implants. These same two authors wished to designate this entity of autoplastic transplantation of splenic tissue as "splenosis."

FIG. 1.

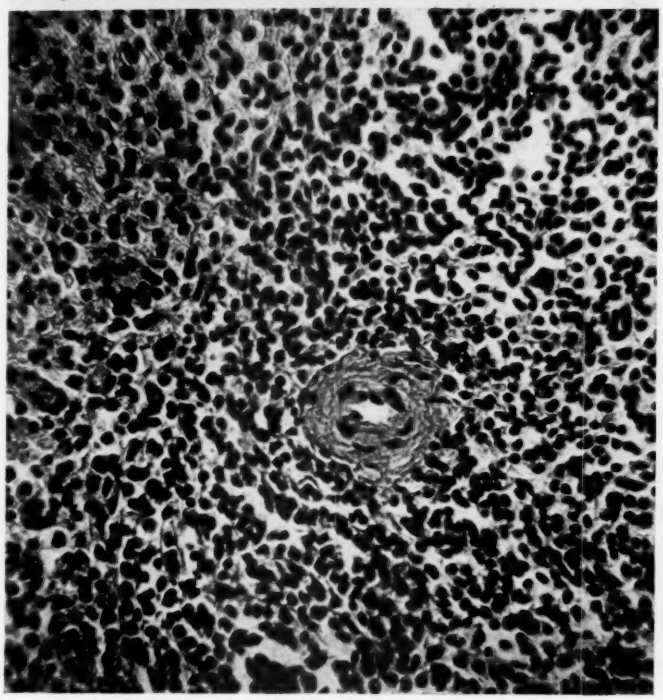

FIG. 2.

FIG. 1.—Photomicrograph of a full-section of autoplastic splenic transplant, from the case reported, showing capsule, trabeculae, malpighian corpuscles, and pulp. On one surface it is adherent to the diaphragm. (Hematoxylin and eosin). (×10)

FIG. 2.—Photomicrograph of the same section as shown in Figure 1 showing a central arteriole, surrounded by lymphocytes, and a portion of splenic pulp. (Hematoxylin and eosin). (×176)

TABLE II

SUMMARY OF REPORTED CASES OF AUTOPLASTIC TRANSPLANTATION OF SPLENIC TISSUE

Author	Date	Sex	Age at Time of Diagnosis	Age at Time of Rupture of Spleen	Reason for Receliotomy	Time after Splenectomy	Location of Nodules	Number	Size of Implants
Albrecht	1896	Male	25	?	Autopsy	No history of trauma or splenectomy	Greater omentum; rectovesical pouch; and both domes of diaphragm.	Numerous	Not stated.
Schilling	1907	Female	47	?	Autopsy	No history of trauma or splenectomy	Greater omentum; peritoneum of anterior abdominal wall; and of pelvis.	42 on great omentum (several more)	Pea to cherry in size.
von Kuttner	1910	Male	?	?	Autopsy	4 years	Scattered throughout the peritoneum.	80 to 100	Not stated.
Foltin	1911	Male	9	3	Chronic appendicitis	6 years	On loops of large and small intestine.	Numerous	Lentil to cherry in size.
von Stubenrauch	1912	Male	?	?	Ileus	10 months	Greater omentum; transverse mesocolon; and small intestine.	Numerous	Hemp seed to pea in size.
Oltman (quoted by von S.)	1919	?	?	?	Not stated	Not stated	Throughout peritoneal cavity.	Multiple	Not stated.
Lee	1923	Male	29	14	Ileus	15 years	Small intestine and mesentery.	Numerous (200–300)	Pin head to 1½ inches.
Kupperman	1936	Male	15	14	Postoperative hernia	6 months	Small and large intestines.	100	Not stated.
Shaw and Shafi	1937	Male	20	?	Autopsy	Not stated	Abdominal wall; pleural cavity; liver; diaphragm; rectovesical pouch; and great omentum.	82	0.2 to 2 cm.
Jarcho and Anderson	1939	Male	8	6	Autopsy (ileus)	18 months	Left dome of diaphragm; liver; stomach; lesser omentum; transverse colon; rt. kidney; rectum; and bladder.	Several dozen	1 to 12 Mm. in diameter. Larger nodules 2 to 3 Mm. in thickness.
Jarcho and Anderson	1939	Male	20	12	Autopsy	8 years	Peritoneum; greater omentum; diaphragm; greater curvature stomach.	80	1 Mm. to 3 cm. in diameter.
Buchbinder and Lipkoff	1939	Female	28	8	Pelvic operation	20 years	Parietal peritoneum; great omentum; ileum; sigmoid; and ascending colon.	Numerous	1 Mm. to 2 cm. in diameter.
Authors	1940	Male	13	9	Autopsy (tetanus)	39 months	Parietal peritoneum; pelvic cavity; omentum; serosa of large and small bowel; diaphragm.	Approx. 75	0.5 to 1 cm. in diameter.

The first group of writers who published case reports, which appear to come in this category, diagnosed the nodules as being either accessory spleens, or tissue derived from embryologic spleen-forming rests, contained within the peritoneum. Spleen-forming rests most likely would be found only in tissues or structures closely approximated to the splenic area in embryologic development. Accessory spleens would be the logical outgrowths from these fetal splenic rests, should they take on a growth stimulus. As to the prevalence of accessory spleens, Adami and Nichols found them in 11 per cent of a series of autopsy examinations. These bodies probably are more often observed in young individuals, than in adults. Jolly states that 25 per cent of children, less than seven years of age, had accessory spleens. Sossuchin observed them in 15 per cent of 153 children, less than ten years of age. Additional mention is made that their diminished occurrence in adult life is possibly due to atrophy. The size of accessory spleens varies from a few millimeters to several centimeters in diameter. Accessory spleens present the same histologic structure, and are subject to the same pathologic alterations, as the main organ. Usually, not more than one to six accessory spleens are present in any one case. These bodies, as mentioned above, are mainly found only in tissues adjacent to the splenic area in fetal development, such as the splenic fossa, gastrolienal ligament, pancreaticosplenic ligament, pancreas, and the great omentum. The large splenic nodule found within the splenectomy bed, at postmortem examination in our case, no doubt, was a true accessory spleen.

The cases reported in medical literature which show splenic implants reveal that these splenic grafts have been found growing on a portion of almost every area of the peritoneal cavity as well as on the contained viscera. In all the reported cases with splenic implants, there are described numerous spleen-like nodules, surrounded by a fibrous capsule of variable thickness, enclosing tissue much like splenic pulp, which may, or may not, have lymph follicles. Any follicles present may be rudimentary in appearance, consisting of a few lymphoid cells surrounding a central arteriole, or they may be well-developed mature follicles. In some instances definite little blood sinus formations are present. Fibrous septa tend to infiltrate the enclosed cellular mass, from the surrounding capsule. A well-developed hilum is absent. The blood supply is from small arterioles which enter the nodule irregularly, from the surrounding tissue, at various points through the fibrous covering. Enveloping the whole nodule is serosa. Apparently, any function that these transplants might have, would be that of the normal splenic pulp.

Grossly, the splenic implants have been found to be both sessile and pedunculated, and to have a nodular, spherical, or flattened shape. They have varied in size from 1 Mm. to 3 cm. in diameter. In color and consistency, the nodules have the appearance of splenic tissue. Colors described for these transplants are normal spleen color, dark red, purple-red, and greenish-black. In one instance, that reported by Buchbinder and Lipkoff, the sur-

geon first discovered many small purple-red nodules, scattered over the peritoneum and viscera during the course of a female pelvic operation, and mistook their appearance for endometriomata, until miscroscopic diagnosis of an excised nodule revealed their true nature. The highest numerical estimate for these transplants was 200-300 in one case. In another instance, the base of the left pleural cavity was invaded. Probably this invasion occurred through a small rent in the diaphragm, which happened at the time of the accident, and later healed. No subcutaneous transplants within the operative wound scar have been reported. However, splenic grafts have successfully taken in the subcutaneous tissues of animals, when experimentally transplanted, as demonstrated by Marine and Manley, Perla, and others.

An interesting case is reported by Jarcho and Anderson, in which about 400 cc. of hemorrhagic blood was removed from the peritoneal cavity, at the time of operation for an acute traumatic rupture of the spleen, and immediately citrated, strained through gauze, and reinjected intravenously into the patient. Eight years later, at the age of 20, the patient died from acute perforated appendicitis. On postmortem examination, there were discovered 80 splenic transplants scattered over the peritoneum but no splenic nodules were found in the lungs, or outside the abdominal cavity. Nevertheless, the possibility of viable splenic cells contained in hemorrhagic blood obtained from the abdomen for retransfusion in such patients should be kept in mind.

Kreuter, in 1920, experimentally excised the spleen in monkeys, and then smeared the splenic pulp over the peritoneum. Several weeks, or months, later, the animals were sacrified, and splenic nodules were found widely dispersed over the peritoneal cavity. Jarcho and Anderson review literature giving instances of dogs who had a history of severe abdominal trauma, and later following death, postmortem examination revealed nodular implants or splenic tissue scattered over the abdominal cavity. These authors also observe that Griffini and Tizzoni, as early as 1883, related that partial splenectomy in dogs was followed by development of spleen-like nodules in the peritoneum.

So far as we were able to ascertain, no cases have been reported in which there were widely disseminated splenic nodules following splenectomy, for nontraumatic diseases of the spleen. Shaw and Shafi express the opinion that the removal of diseased spleens, apparently is rarely, if ever, followed by implants, in spite of occasional tearing, with some associated hemorrhage, during the excision of large splenomegalies.

In the spleens of individuals, past the age of 30, Gross finds that the nuclei of the fibroblasts disappear, and the fibrils become thickened and few. Likewise, the intima and media of the blood vessels within the parenchyma become thickened with connective tissue, and hyaline changes. Wohl calls attention to the gradual collapse of lymph tissue, from birth onward. Because of the changes, mentioned above, he believes there occurs a decrease

in the power of constructive metabolism, which factor contributes to the rather early senescence of the organ.

The average known age at the time of the traumatic rupture of the spleen, among all the reported cases of autoplastic transplantation of splenic tissue including ours, was nine plus years. It appears to us quite significant that the youngest was age three, and the oldest was 14 years. We believe the likelihood of successful grafting of these cells on a peritoneal surface is proportionate to the youthfulness of normal splenic tissue which has been traumatically ruptured. Pulp cells from the spleen of young individuals, very likely, possess properties of increased viability, or virulence, differing from similar cells in the adult spleen. We are of the opinion that such splenic implants may be found more often after traumatic rupture of the spleen, in young individuals who survive, than is generally recognized, and probably such a response is more the rule than the exception.

As yet, no symptoms have been known to result from these splenic implants. That the opportunity offered to discover such a condition in man, is minimum, was remarked in the early part of this discussion. Jarcho and Anderson, more concretely, emphasize this circumstance in their review of the last 2,000 autopsies at the Babies Hospital in New York, by finding only nine cases who had undergone a previous splenectomy for various reasons, from a few hours to nine years prior to autopsy. The only case in which operation had been performed, because of traumatic rupture of the spleen, was one of their published cases of autoplastic transplantation of splenic tissue. Then again, out of 2,605 autopsies at the Presbyterian Hospital, in New York, during a ten-year period, these same authors found that splenectomy had been performed in 16 cases, from two weeks to 16 years, prior to autopsy. There were no instances of splenectomy for traumatic rupture of the spleen in this group, and none revealed splenic tissue, other than the finding of an accessory spleen, or so, in the bed from which the spleen had previously been removed. Finally, Shaw and Shafi observe that out of a series of 708 cases of splenectomy, published up until 1908, and 417 cases reported by Mayo in 1926, no pathologic studies of the late results of splenectomy are mentioned.

SUMMARY AND CONCLUSIONS

(1) A human case is reported which developed nodular splenic implants throughout the peritoneal cavity, following traumatic rupture of the spleen. This is the thirteenth case of similar nature, in man, described in medical literature. A chart summarizing these cases is appended.

(2) A detailed discussion of autoplastic transplantation of splenic tissue, is made.

(3) It is our opinion, that in man relative youthfulness of normal splenic tissue is a very important factor, as regards viability of splenic pulp cells for autoplastic implantation, and the likelihood of successful grafting of these cells on a peritoneal surface following traumatic rupture of the spleen.

(4) Autoplastic transplantation of splenic tissue may be more the rule than the exception in individuals who have suffered a traumatic rupture of the spleen, in their youth, and have survived the accident.

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AN UNUSUAL CASE OF BENIGN MULTIPLE CHORIONIC VILLI IMPLANTS IN PERITONEAL CAVITY ACCOMPANIED BY HEMOPERITONEUM

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TO CLEARLY UNDERSTAND the significance of the case about to be reported, it would not be amiss to review the subject of chorionepithelioma. Chorionepithelioma is a malignant tumor originating from, and confined to the epithelium of the chorionic villus, which differs from the hydatid mole in that in the latter there also occurs an accompanying proliferation of the villus stroma. As is well known, this neoplasm may arise from the chorionic villus at term, in cases of abortion or from an hydatid mole. While the usual site of growth is the uterine cavity, it has been known to take origin in the fallopian tube (Walsh,[20] Phillips,[12] Moore[11]). In rare instances the site of origin could not be determined, since the uterus and adnexa have been found normal in cases where the manifestations of the disease resulted from distant metastases. In a few cases the site of origin of the chorionepithelioma has been a teratomatous tumor in an ovary or testis.

While Chiari,[2] as far back as 1877, was the first to describe three cases of carcinoma of the uterus which have subsequently been classified as chorionepitheliomata, it was not until 1895 that Marchand[9] first recognized that such tumors were of epithelial nature and that their site of origin was the placenta.

Pregnant women during childbearing period are most frequently affected. Cases, however, have been reported during the menopause, and in rare instances in young virgins. Several cases have also been reported in the male where the tumor has taken its origin in a teratoma of the testis. A review of the literature disclosed the fact that in the great majority of cases, the tumor manifests itself between one and four months after full term labor, abortion, or the expulsion of a mole.

The characteristic feature of an uterine chorionepithelioma is a nodular or fungating, friable tumor presenting a distinctly hemorrhagic appearance, with evidence of infiltration of the uterine wall. The tumor may penetrate the wall of the uterus and invade the peritoneum. The macroscopic appearance of an extra-uterine chorionepithelioma is that of a tumor resembling an hematoma, presenting no anatomic relationship to the site of a preexisting placenta, located anywhere in the peritoneal cavity, portio vaginalis, broad ligament, or the vagina. The general consensus of opinion is that such a tumor probably arises from a primary uterine tumor which has either undergone regression or has been expelled with its placenta. von Zalke,[19] however,

states that such extra-uterine chorionepitheliomata may arise from cells which have been extruded through the tube from a possible normal intra-uterine placenta. Cases have also been reported of chorionepitheliomata arising in the fallopian tubes (Georgii,[7] Solomons and Smith[16]).

Sunde[18] reported a case of chorionepithelioma arising from an ovarian pregnancy. Pick,[13] discussing the problem of ovarian chorionepithelioma, maintains that, as a rule, such tumors arise from preexisting teratomata, without the presence of pregnancy.

In differentiating between the histologic features of the constituents of a normal chorionic villus and that of a villus from a chorionepithelioma, we find in the latter that the cells show a greater tendency to invade blood vessels, to produce a ferment with properties of causing tissue dissolution, and to cause vasodilatation of surrounding capillaries. Both types of villi contain Langhans' cells and syncytium, and it was Marchand[9] who first proved that the chorionepithelioma took origin from the trophoblast.

Microscopically, a typical chorionepithelioma discloses Langhans' cells which appear as well circumscribed polygonal cells with large nuclei. Among these cells one sees groups of darker-staining multinuclear cells or sheets of cells—syncytium, along with numerous blood sinuses, some of them containing tumor elements. Hemorrhagic islands and areas of scattered necrosis are characteristically seen in these tumors. Rarely does one encounter well-defined villi in chorionepitheliomata. Alveolar arrangement of the cell groups makes up the usual mosaic of such tumors. Invasion of surrounding musculature is readily discernible by the presence of islands of tumor cells dispersed among the muscle fibers. The presence of old blood, fibrin and leukocytes can be seen surrounding the site of the tumor. Invasion of the existing blood vessels by tumor tissue is not uncommon. Tumors vary widely in their contents of Langhans' cells and syncytium, some chorionepitheliomata having a preponderance of Langhans' over syncytium, and *vice versa*. In contradistinction to the normal chorionic villus, one notes in chorionepitheliomata a greater variation in the size, shape and staining qualities of the individual Langhans' cells and a greater likelihood of mitotic figures within the cell nuclei.

Although Ewing[3] maintains that one can give a fairly accurate prognosis based upon the histologic features of a given tumor, the consensus of opinion to-day is that such histologic groupings are unreliable as a prognostic index (Schlagenhaufer,[15] Frank,[5] Frank and Geist[6]).

Chorionepithelioma is notorious for its tendency to metastasize early. This is due to the close proximity of the tumor tissue to blood sinuses and to the marked tendency of the neoplastic tissue to invade blood vessels. The sites of predilection of such metastases are the lungs, vagina and vulva. The histologic structure of metastases closely simulates that of the parent tumor, and only in rare instances have distinctly formed villi been found (Miller[10]).

Uterine bleeding is by far the outstanding symptom of chorionepithelioma, and may appear during or after the termination of pregnancy. At times,

bleeding may be severe enough to cause exsanguination and death, but, usually, bleeding is more or less intermittent. Cases have been reported where the initial symptoms manifested themselves as a result of metastases (Kedzierski,[8] Straume[17]). In any event, the persistence of vaginal bleeding following a miscarriage or a normal labor should arouse suspicion that such a condition might be present. A carefully performed currettage definitely establishes the diagnosis.

At the present time, great reliance is being placed upon biologic tests to determine the presence and course of a given case of suspected chorionepithelioma. Frank and Geist[6] report no false positive reactions in their extensive experience with the Aschheim-Zondek test in mice, or with the Friedman tests on rabbits. However, in less than two per cent of their cases these same investigators have noted a negative reaction which turned positive after an interval of two or more weeks.

While it is true that the diagnosis of chorionepithelioma usually carries with it a grave prognosis, one must be extremely guarded in following this rule in a given case, since it is well known that the disease discloses great variation in its virulence. Cases have been reported where the disease followed a fulminating course, while others have been noted to show spontaneous regression (Rockafellow[14]). Such variations in behavior of chorionepithelioma may of course have been due to errors in properly interpreting histologic sections. With the present use of biologic tests, however, such errors will most likely be greatly avoided. According to Frank and Geist,[6] the most virulent tumors are those originating in the fallopian tube, ovary and testis.

Case Report.—M. L., age 23, was seen in consultation on February 18, 1940, complaining of severe pain and tenderness in the lower abdomen of one day's duration.

The family history was irrelevant. Two years previously she had been delivered of a dead fetus, at term. Following the delivery her periods returned to normal, until December 20, 1939, when she skipped a period. This amenorrhea was attributed to pregnancy and an abortion was performed January 20, 1940. There was no staining or bleeding following the currettage. On and off, for the past three months, she complained of pain in the lower abdomen. For the preceding 24 hours, however, the pain in the abdomen had become severe and was accompanied by nausea.

She was admitted to the hospital February 18, 1940, where a physical examination disclosed a pale, poorly nourished young woman, appearing acutely ill. Save for the abdominal and vaginal findings, the physical examination was essentially negative.

Abdominal examination disclosed a moderately tender, soft abdomen, with a positive rebound. Vaginal examination disclosed a small, apparently normal, freely movable uterus, with suspicious fluctuation in both fornices. Temperature 99° F.; pulse 80. Leukocytes 16,300, 88 per cent polymorphonuclears, and 12 per cent lymphocytes. The urinalysis was essentially negative. Suspecting that we were dealing with a surgical abdomen, probably due to an acutely inflamed appendix, celiotomy was advised and accepted.

Operation:—Under spinal anesthesia (tropacocaine), the abdomen was opened through a three-inch right lower Kammerer incision. Upon incising the peritoneum, one noted a large amount of blood and several large clots in the peritoneal cavity. The uterus appeared small, was of normal consistency, and to all intents and purposes normal in every

way. The left adnexa disclosed a few, small bead-like nodules on the outer surface of the tube, but appeared otherwise normal; while the right fallopian tube was studded with small dark-purplish nodules, giving the tube the appearance of a string of colored beads. The ovary was closely adherent to the tube, but one could not ascertain any distinct evidence of rupture either of the tube or ovary to warrant the assumption that we were dealing with a ruptured ectopic pregnancy. Blood, however, seemed to be oozing from the right tube.

After thoroughly evacuating the peritoneal cavity of blood and clots, one noted several nodules of a dark-purple color, varying in size from beads to small hazel nuts, studding the serosa of the small and large bowel and omentum. The appendix appeared slightly injected and thickened, with a bulbous tip. The right tube and ovary were extirpated along with the appendix. A portion of omentum containing a few large nodules for histologic study was also removed between mass ligatures. The abdomen was closed in layers.

Postoperative Course:—On the evening of the twenty-second, 450 cc. of citrated blood was administered intravenously. Save for a feeling of marked asthenia, the postoperative course was uneventful. A blood count, taken February 26, showed 4,000,000 R.B.C.; 7,700 W.B.C., with 60 per cent polymorphonuclear leukocytes, and 40 per cent mononuclear cells; hemoglobin 70 per cent. Two days later the hemoglobin rose to 82 per cent. The wound healed by primary union and the patient was discharged March 2, 1940.

An Aschheim-Zondek test taken while the patient was still in the hospital was positive. Four successive A-Z tests performed subsequently, at weekly intervals beginning March 5, 1940, were all negative.

Pathologic Examination.—Gross: Dr. A. Schifrin. Specimen consists of two masses: (1) A portion of omentum measuring 7x4 cm. There are four hemorrhagic, spherical masses present, varying from pea- to cherry-size. On section they consist of clotted blood within which no cellular tissue is noted grossly, except for occasional greyish-pink dot-like fragments of friable tissue. The peripheral zone fuses with the areas of interstitial hemorrhage. In adjacent portions there are fibrinous adhesions and curling of the omental surface. (2) A tube and ovary with tubo-ovarian ligament. The ovary is the size of a walnut and is but slightly enlarged. The surface shows several split pea and smaller hemorrhagic nodules which, on section, seem to be superficial and do not seem to arise from within the ovary. The ovarian parenchyma shows fibrosis and several follicular cysts and involuting corpus luteum. The tubo-ovarian ligament contains a pea-sized and several smaller nodules which are fully covered by the peritoneal reflection. The latter appears bluish but not ulcerated or perforated. On section, the nodule consists of an hemorrhagic, rather well-localized mass which contains greyish-pink cellular tissue. This mass is not in communication with the tubal lumen but is in contact with the outer wall of the latter. There are several similar smaller nodules, some close to the peritoneal reflection, but more penetrating it. The tube is of normal size, slightly edematous; and the lumen contains pale white mucosal folds which fill the latter. The lumen is not dilated and contains no blood. The fimbriated extremity is normal.

Microscopic.—Omental Hemmorrhagic Mass (Fig. 1): This mass is the largest of the omental masses and is 2.5 cm. in diameter. Its central portion is occupied by clotted blood consisting of dense platelet masses and extravasated intact red blood cells with scattered polynuclear leukocytes and lymphocytes. Within the meshes of the clot, typical degenerated chorionic villi are seen composed of a central zone of myxoma-like stroma with poorly staining nuclei and a bright pink peripheral syncytial layer containing occasional necrobiotic and pyknotic nuclei. At the periphery of the bloody mass there are more typical chorionic villi which, however, are intact and stain well. They consist of a central zone of loose myxoma-like stroma with well-stained, spindle-shaped and vesicular nuclei. The peripheral layer of the villi is composed of a single row of cuboidal-

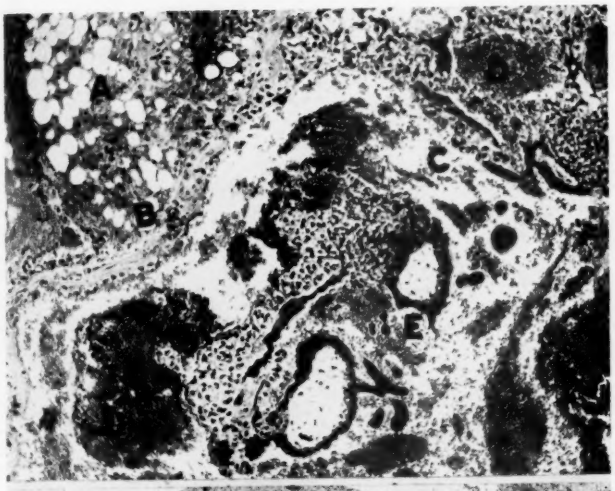

FIG. 1.—Section from larger hemorrhagic omental mass. (A) Omental fat tissue showing interstitial hemorrhage and mild fibroblastic, round cell and leukocytic reaction. (B) Wall of the mass showing fibrosis and scant decidual reaction. (C) At left and above, several chorionic syncytial elements with regular nuclei. (D) Extravasated blood with darkly-staining chorionic wandering cells at left, and pale decidual cells above D. (E) Two well-formed, typical chorionic villi with regular Langhans' and syncytial cells.

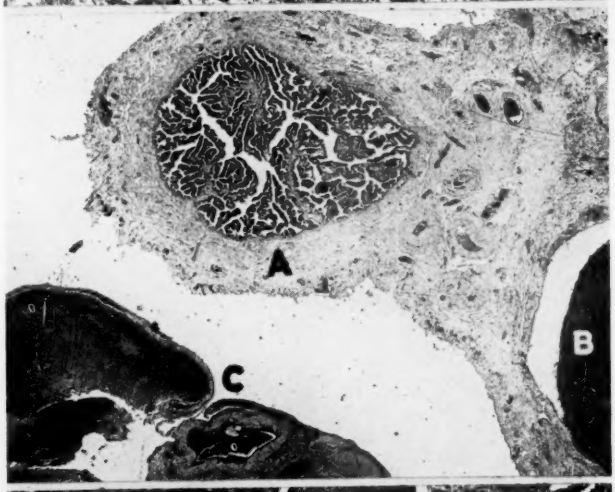

FIG. 2.—Section through fallopian tube, tubo-ovarian ligament and ovary (bird's-eye view). (A) Cross-section of tube showing absence of tubal pregnancy. (B) Cystic, hemorrhagic nodule containing clotted blood. Chorionic elements such as is seen at D were present. (C) Hemorrhagic nodule at surface of ovary showing chorionic villi directly below C.

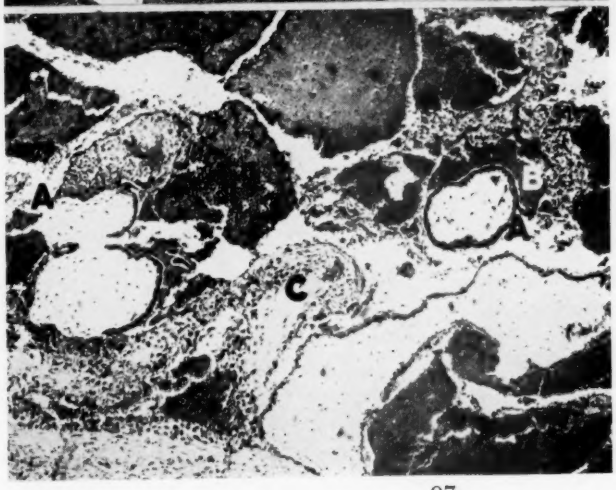

FIG. 3.—Section through another nodule in tubo-ovarian ligament. (A) Two well-formed chorionic villi showing very regular Langhans' cell layer and loose, intact stroma and absence of hydatid mole stromal changes. (B) Syncytial cells above and below B, containing regular nuclei. (C) Pale decidual cells with regular nuclei.

like cells with regular, uniform, round, oval or flattened vesicular or dense nuclei (whose diameter is about one and one-half to two times the diameter of a red cell). This row of cells is continuous with a layer of syncytial cells whose cytoplasmic borders are indistinct and whose cytoplasm is intensely pink and finely granular. These syncytial cells are multinucleated, being composed of several vesicular or dense, well-staining regular nuclei (whose diameter is about two times that of a red cell). These syncytial cells form the bud-like blunt ends of the villus. Their nuclei are regular, occasionally slightly larger, but not at all bizarre, atypical or mitotic. Where the chorionic villus is seen to be in contact with the delimiting wall of the mass, the wall contains large, pale, polygonal decidual cells, with abundant clear pale cytoplasm and well staining vesicular or solid regular nuclei. Their cytoplasmic borders are usually distinct and the cell aggregates have a mosaic-like appearance. These decidual cells are in continuity with, and lie freely within the delimiting wall which is otherwise composed of fibroblastic and fibrous connective tissue containing numerous hyperemic blood capillaries and arterioles and showing interstitial hemorrhage and focal infiltration by round cells. The outermost portion of the delimiting wall consists of the adipose tissue of the omentum. The latter also shows hyperemic large blood vessels and interstitial round cell infiltration, especially perivascularly. Of note is the absence of chorionic villi external to the delimiting fibrous zone and the absence of such elements from the numerous surrounding blood vessels. The mosaic-like decidual reaction in some of the septa near adjacent vessels is, however, quite prominent.

Several Similar Hemorrhagic Masses in Omentum: These are of varying size, all being smaller than the mass described above. These masses are hemorrhagic nodules with fresh and clotted extravasated blood, some contain typical chorionic villi with well-staining, regular nuclei. The delimiting wall is thinner and contains an occasional larger (four times diameter of red cell) loculated nucleus such as is seen in chorionic wandering cells. The chorionic nuclei show no mitoses. There is definite but scantier decidual reaction or decidual cell mosaic structures. The adjacent blood vessels also show marked perivascular round cell infiltration.

Tube, Ovary and Tubo-ovarian Ligament (Figs. 2 and 3): The small hemorrhagic areas on the surface of the ovary are devoid of a serosal covering, which is seen overlying the surface of the adjacent portion of the ovary in the form of a row of cuboidal cells. These hemorrhagic nodules have the appearance of surface implants rather than intra-ovarian structures which have penetrated the surface. The latter opinion, however, is not entirely excluded, as some nodules lie definitely below the surface and are covered by a portion of ovarian stroma covered by cuboidal serosal cells. Within the parenchyma there are several small follicular cysts lined by a thin resting layer of regular thecal cells with scant cytoplasm and no evidence of lutein cell formation. Nearby there are present granular lutein cells with polygonal cytoplasmic borders, giving the decidual-like appearance to them. The fallopian tube is entirely intact. The lumen is not dilated, nor does it contain blood or placental tissue. The mucosal folds are regular, lined by regular columnar cells. The stroma of the folds is delicate and shows no decidual reaction. The muscular layer is distinct. Where the tubo-ovarian ligament fuses with the tubal wall, however, the arterioles and veins are prominent. About these vessels there is prominent round cell infiltration and the adjacent stroma shows edema, hyaline change and chorionic villi which lie freely within the stroma as if penetrating the latter. These chorionic villi are well formed with regular nuclei and are closely situated to the hemorrhagic nodule within the ligament which contains numerous regular chorionic villi with regular nuclei. The wall of this nodule is not entirely delimited and shows decidual cells. Chorionic wandering cells are present but not too bizarre or mitotic. Thus, all the hemorrhagic nodules contain decidual and chorionic tissue with rather regular nuclei and some chorionic wandering cells. Some of the nodules are well delimited, others show penetration of the villi into the adjacent tissue. Mitoses are very rare; atypism is scant. Of note

is the absence of prominent solid cellular tumor-like masses such as is usually seen in chorionepitheliomatous invasion. *Pathologic Diagnosis:*—(1) Multiple hemorrhagic nodules within omentum, tubo-ovarian ligament and ovary. (2) Superficially implanted hemorrhagic nodules in ovary. (3) These nodules contain chorionic villi and decidual tissue with rather regular nuclear structures and show chorionic wandering cells and villus penetration into adjacent tissues. (4) Frank nuclear atypism, bizarreness and prominent mitoses or solid tumor-like aggression, such as is commonly seen in the usual chorionepithelioma are absent. (5) The fallopian tube itself contains no decidual or chorionic tissue within it.

COMMENT.—From the macroscopic appearance the nodules suggested multiple (malignant) chorionepitheliomatous metastases. Histologically, however, they failed to show the typical aggressive cellular bizarreness of the usual metastasizing chorionepithelioma or hydatid mole and could possibly be interpreted as being unusual implants from an intra-abdominal pregnancy which had ruptured. The classification of this case is not as yet fully settled, as it shows border-line features. For the present, it is best classified as showing multiple chorionic tissue implants with a strong (though not purely histologic) suspicion requiring further observation by A-Z tests and clinical course to exclude the possibility of a truly malignant metastasizing chorionepithelioma.

When last seen, March 26, 1940, the patient felt well and presented an hemoglobin of 88 per cent. The uterus felt small and normal, and there was no evidence of uterine bleeding.

Discussion.—In carefully reviewing the sequence of events in this case, we find a young woman who, two years previously, went through an apparently normal pregnancy, giving birth to a dead fetus. Up to three months prior to her present illness, she was free of abnormal symptoms. From that time on, she complained of vague abdominal pain. Slightly less than four weeks prior to operation she was curretted for a supposed intra-uterine pregnancy, having missed one period. Although she complained of abdominal pain on and off for three months, it was only during the 24 hours preceding operation that the pain became acute. Operation revealed a great deal of blood and many clots in the peritoneal cavity. The tubes and ovaries, particularly the right, were studded with small nodules but presented no rent indicative of a ruptured ectopic. There were a number of nodules covering the serosa of the cecum and ileum and several dark-purplish nodules varying in size from beads to small hazel nuts. A section of omentum removed for histologic study disclosed the tumors to consist of typical chorionic villi with features suggesting distinct variation from chorionepithelioma. The benignity of the lesion was more or less confirmed by the fact that four subsequent Aschheim-Zondek tests were all negative.

Two pertinent questions arise in this case: First, where was the site of the original pregnancy; was it in the tube, was it in the uterus, or was it intra-abdominal? Second, in which way does the histologic architecture of this tumor differ from that of a true chorionepithelioma?

Regarding the possibility of the uterus being the original site of preg-

nancy, all that can be stated, at present, is that, at operation, the uterus appeared and felt perfectly normal. Unfortunately, a currettage was not performed at the time of operation or immediately after to absolutely rule out this possibility. Since the lumen of the left tube was found to be apparently normal, this source can logically be eliminated as a possible site. The involved right tube and ovary, after a thorough histologic study, failed to reveal any evidence of placental tissue within the lumen of the fallopian tube. This leaves the third possibility—that the pregnancy might have been intra-abdominal. It is quite possible that the fetus might have escaped detection because of the fact that the intra-abdominal clots which were removed with moist sponges were not recovered for examination. This possibility is, however, somewhat remote since one can scarcely conceive of an intra-abdominal pregnancy being present which could, by light swabbing, be removed from its attachment.

Regarding the differential diagnosis between the case here presented and chorionepithelioma, one must fall back upon histologic and biologic criteria. A careful examination of the photomicrographs, here presented, will disclose well differentiated villi which are not commonly seen in cases of chorionepitheliomata, but which characterize normal chorionic tissue. Furthermore, the cells here seen are typical Langhans' syncytial cells with scant evidence of the nuclear mitoses, atypism or bizarreness so frequently encountered in chorionepitheliomata. In addition, one sees little evidence in any of the sections of invasion of the blood spaces by chorionic tissue which is so frequently evident in the malignant type of tumor. Taking the entire picture of the histologic structure of the tumor here presented, and comparing it with that of a typical chorionepithelioma, we are struck with a sufficient number of variants to warrant its classification among the benign rather than among the malignant tumors.

A careful review of the literature has, to date, failed to reveal an exactly similar instance of benign multiple chorionic villi intra-abdominal implantations.

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KRUKENBERG'S TUMORS*

A SURVEY OF FORTY-FOUR CASES

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KRUKENBERG,[21] in 1896, described five cases, and a specimen of ovarian malignancy, that showed a peculiar and poorly understood gross and microscopic picture. Grossly, the tumor was of moderate size; it was nodular yet it possessed a smooth surface. Adhesions were usually absent in such cases but ascites was often found. The tumor was usually bilateral, usually solid, occasionally cystic and the general form of the normal ovary was usually maintained. The cut surface had a myxomatous appearance. Microscopically, Krukenberg described "signet-ring" cells surrounded by a fibrous stroma. He recognized the picture as one of undoubted malignancy and considered the lesion as primary in the ovaries. He classified it among the sarcomata but in the title of his thesis, *"Über das Fibrosarcoma Ovarii Mucocellulare (carcinomatodes),"* he obviously entertained the possibility of its origin from epithelial cells. No one has yet given a better description of this tumor than he.

Although tumors of this type now bear the name of this early investigator, historical researches reveal that he was not the only pioneer in this particular field of research.[1, 35]

Important contributions were made by Waldeyer,[37] in 1872, and Welch,[38] in 1892. Knowledge of the epithelial origin and secondary nature of the lesion is due chiefly to the observations and writings of Schlagenhaufer,[33] Wagner,[36] Glockner[15] and Römer.[30] Other important contributions have been made by Major,[25] Fallas,[12] Hundley,[18] Woodall,[39] Jarcho,[19,20] Masson,[26] Shaw,[34] Novak and Gray,[28] Horsley[17] and others.[16]

Histogenesis.—Since the lesion was shown by the above mentioned writers to be secondary in most instances, all workers have agreed on this one fact. However, there is as yet no general agreement as to what constitutes a Krukenberg tumor; as to how metastasis occurs; as to whether a primary ovarian carcinoma may be impossible to distinguish from a Krukenberg

* Abridgment of thesis submitted by Dr. Leffel to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Surgery.

tumor; as to whether the metastasis is in any way selective; or on how the lesion should be treated.

Novak and Gray, Ewing,[11] and many others have expressed the belief that all or most of the original criteria set down by Krukenberg's description should be fulfilled. Jarcho, on the contrary, pointed out the great variation in the appearance of these tumors and stated that "signet-ring" cells are not always found. Most authors believe that the primary lesion, in these cases, must be a "colloid" or mucus-containing carcinoma. Novak and Gray, Jarcho, and Larson,[22] however, do not agree. There is no agreement in the literature as to how metastasis occurs. Novak and Gray, Shaw,[34] Broders,[9] Armstrong and Wolfe,[3] Runyeon[31] and many others have said that spread is usually by way of the lymphatic system. Others stress the possibility and probability of spread by peritoneal sedimentation. Boyd[4] belongs to this latter school of thought. Major[25] reported a case in which carcinoma cells were found in the pulmonary blood vessels. This, he felt, was very suggestive that hematogenous spread occurs. That spread may occur by contiguity is probably conceded by all.

Cases of primary ovarian adeno-"colloid" carcinoma resembling microscopically Krukenberg's tumor have been reported by Schenk,[32] Glockner,[15] Frankl,[14] Neumann,[27] Outerbridge,[29] Andrews[2] and others.

As to what surgical treatment should be instituted in these cases, great disagreement exists. Comando[10] and others have expressed the belief that in the absence of gross generalized carcinomatosis both the primary growth and the ovaries should be removed. An opposite view is expressed by those who think that all surgery is contra-indicated. MacCarty,[23, 24] speaking principally of primary ovarian carcinoma, has pointed out the importance of removing the uterus and tubes as well as the ovaries, to prevent recurrence in the pelvis.

Materials, Methods and Purpose of Present Study.—Our material for study consists of 44 cases encountered at the Mayo Clinic from 1908 to 1938, inclusive. Five of the cases have previously been studied and reported by Masson.[26] Case histories were abstracted, surgical and postmortem material has been examined, and all available tissue has been studied microscopically. The presence of mucus in the primary and metastatic lesions was demonstrated by means of the Galantha stain for mucus. In 19 of the 44 cases, only surgical material and surgical records were available. In the remaining 25 cases surgical material plus complete postmortem material was available.

We wish to present our views on four important questions: (1) What is a Krukenberg tumor? (2) By what route does metastasis occur? (3) Does a primary adeno-"colloid" carcinoma of the ovary ever mimic a Krukenberg tumor? (4) What surgical procedures are indicated in dealing with these cases?

Clinical Observations.—The average age of the patient when the ovarian lesion was found was 48.2 years. All except four of the patients were, or had been, married. One patient was a Negro; all the others were white persons. There was nothing typical about the case histories.

Ascites was recorded in 17 instances and absent in 27. Both ovaries were involved in 35 cases, and in nine instances unilateral involvement was found.

In 30 instances, the diagnosis of the original lesion was made first. In 14, the secondary lesion was diagnosed first, and in all but three cases the original lesion was found at celiotomy or postmortem examination. The primary lesion was found in the stomach in 20 instances; in the sigmoid or rectosigmoid in seven; in the colon in four; in the gallbladder in three; in the cecum in two; in the jejunum in two; in the uterus in one; in the breast in one; in the hepatic duct in one; and in three cases, without postmortem study, the site of the original lesion was not definitely found (Table I).

TABLE I

FINDINGS IN FORTY-FOUR CASES OF KRUKENBERG'S TUMOR

Primary Lesion		Nature of Metastatic Involvement					
Site	Frequency	Bilateral Ovarian	Peritoneal Implant	Periaortic Nodes	Generalized Carcinomatosis	Ascites	Average Postoperative Life (in months)
Stomach	20	17	9	5	12	10	9.8
Sigmoid (rectosigmoid)	7	6	4	2	5	1	12.8
Colon	4	2	2	2	2	0	3
Gallbladder	3	3	2	1	2	2	2.5
Cecum	2	1	1	1	1	0	0.5
Jejunum	2	2	2	1	2	1	0.25
Uterus	1	0	0	0	0	0	0.75
Breast	1	1	0	1	1	0	0.5
Hepatic duct	1	0	0	1	1	0	2
Unknown	3	3	2	0	2	3	4
Totals	44	35	22	14	28	17	3.61

Pathologic Observations.—Our description of the gross characteristics of the larger Krukenberg tumors that we studied would only repeat the excellent description written by Krukenberg. The largest tumor that we encountered was approximately 24 cm. in diameter; the smallest was the size of an atrophic ovary. All of the tumors that we studied had a smooth capsule, were free of adhesions, and possessed an irregular nodular contour. Associated cysts were often found. There was a striking tendency for the tumor to maintain the general form of a normal ovary. In our experience, there was not always gross evidence of other metastasis. The cut surface of the tumor had a myxomatous appearance. After a time the substance of the tumor showed a tendency to recede, leaving a concave rather than a convex cut surface. Regions of necrosis were often encountered.

Microscopically, the epithelial elements composed of large rounded or polyhedral cells were seen in groups of varying size, intimately mingled with the fibrous stroma. The epithelial cells were in some instances forming well-defined glands; in others no glandular arrangement could be seen, but rather the appearance was that of wild cellular proliferation (Fig. 1). Interestingly enough, the above variation was seen not only in different sections of the same tumor but also in different regions of the same section (Fig. 2). The nuclei of the epithelial cells were usually displaced peripherally and compressed by mucus giving rise to the "signet-ring" appearance. The fibrous

stroma varied but little, being quite dense in a few regions, but in most, loose and edematous. Little has been written regarding the stromal reaction when the ovary is invaded by a carcinoma. The loose areolar-like stroma lying between regions of dense stroma seemed to us almost constant.

COMMENT.—What constitutes a so-called Krukenberg tumor? The views of others already have been given herein. With the view that all or most of the original criteria in Krukenberg's original description must be fulfilled, we whole-heartedly disagree. It is our feeling that the criteria for the

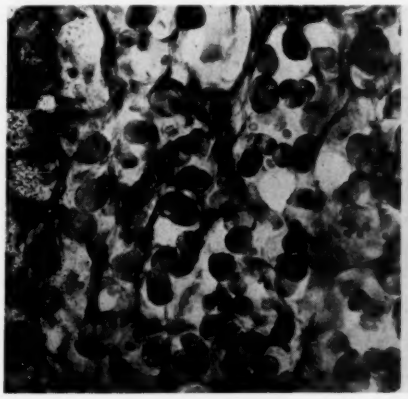

FIG. 1.—Typical microscopic picture of Krukenberg's tumor. (×275)

(a) (b)

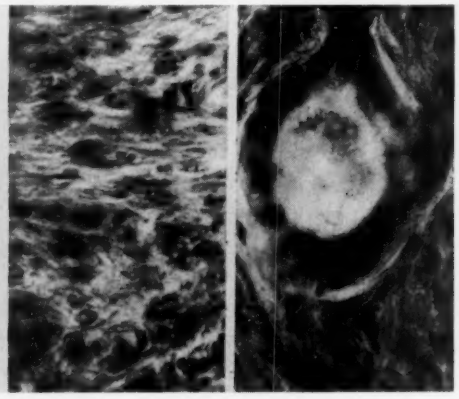

FIG. 2.—Krukenberg's tumor; (a) section showing complete lack of differentiation; (b) section of same tumor showing glandular formation. (×465)

classification of a particular pathologic finding must be such that all like lesions can be included. There is one constant finding in Krukenberg tumors and that is mucus in the epithelial cells. As previously mentioned there are those who state that "signet-ring" cells are not always found. It is true that their prominence varies greatly but in our experience careful search nearly always reveals some of them. At any rate, all will agree that mucus-containing cells are the most constant finding. All the other typical findings fail to be present in some cases. It is true that most metastatic adeno-"colloid" carcinomata of the ovary, by the time they are diagnosed, appear similar grossly and microscopically to the tumor which Krukenberg described. However, that a lesion has not had ample time to manifest a gross pathologic picture is no reason for its not being properly identified. A few metastatic "signet-ring" carcinomatous cells in the cortex or hilus of an ovary constitute a Krukenberg tumor just as does a similar tumor the size of a child's head (Fig. 3). The former needs only time to mimic the latter. Ewing suggested that lesions showing acinar structures should be excluded. However, serial sections will reveal acinar structures in a high percentage of all so-called Krukenberg tumors. As previously stated it is interesting how both types of pictures can be seen in the same section (Fig. 2). An ovary involved secondary to a low grade adeno-"colloid" carcinoma of the colon shows a great deal of acinar structure, yet it is not different from an ovary

involved secondary to a high grade adeno-"colloid" carcinoma of the stomach which shows a very little acinar structure. Each of these types of ovarian lesion is a metastatic adeno-"colloid" carcinoma of the ovary. We feel that these tumors should be described, like other metastatic tumors, merely as metastatic carcinoma of the ovary. Realizing, however, that the term "Krukenberg's tumor" will continue to flourish in medical literature, we contend that it should include all metastatic adenocarinomata of the ovary. There is no real difference between metastatic adenocarcinoma of the ovary and metastatic adeno-"colloid" carcinoma of the ovary, save for the presence of mucus in the latter. However, if this difference were overlooked, not even the remotest reason would ever exist to use the term "Krukenberg's tumor."

Whether or not the presence of mucus can always be demonstrated in the primary lesion we do not know. It already has been pointed out, herein, that some workers report finding adeno-"colloid" carcinoma in the ovary secondary to a primary adenocarcinoma, which contained no mucus. This was not our observation. In every instance in which it was possible to examine the primary lesion there was definite evidence of the presence of mucus therein. The amount of mucus in the primary lesion roughly varied inversely to the grade of the carcinoma, graded by Broders'[5-8] method on the basis of one to four.

By what route does metastasis occur? There are four possibilities that we wish to consider: (1) Spread by peritoneal sedimentation; (2) spread by lymphatic channels, which must include retrograde spread; (3) extension by continuity; and (4) spread by way of the blood stream.

Two reasons have been advanced for believing that spread may occur by means of peritoneal sedimentation: (1) Carcinoma cells are frequently found in peritoneal fluid in cases of abdominal carcinomatosis. (2) Early involvement of the ovarian cortex without involvement of the ovarian medulla is occasionally seen (Fig. 3).

Certainly no one will question the first reason. If carcinomatous cells are present in the fluid there is no reason why they should not attack the ovary just as they may and do attack other structures. What depth the primary lesion must reach in the involved wall, so that carcinoma cells may invade the peritoneal fluid we do not know.

The second reason we admit is open to question. One does occasionally encounter involvement of the ovarian surface or cortex but does not find involvement of the ovarian medulla or hilus. We have one such case (Fig. 3). By what mechanism the germinal epithelium is permeated, if it is, we do not know.

Another reason, listed by some, as previously mentioned, is the high incidence of peritoneal implants in these cases. This certainly is not evidence against the possibility of this type of spread but it must be remembered that, as Broders[9] has pointed out, the peritoneum contains a network of lymphatic vessels. Spread along these vessels with occasional involvement of the peritoneal surface would produce a picture similar to that described by

Boyd.[4] We do not know that this ever happens but we do know that carcinoma cells invade the peritoneal lymphatic vessels. Figure 4 illustrates a peritoneal lymphatic vessel loaded with carcinomatous cells.

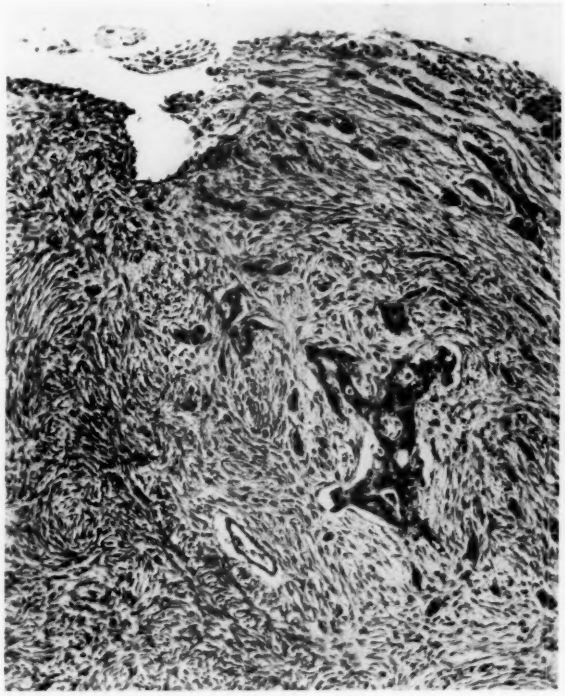

FIG. 3.—Tiny metastatic nodule at periphery of ovary—one may note break in the continuity of the germinal epithelium. (×85)

We feel, therefore, that since carcinomatous cells are frequently found in peritoneal fluid it is logical to conclude that metastasis by peritoneal sedimentation may occur. The occurrence of involvement of the ovarian surface, in the absence of other ovarian involvement, adds to this hypothesis. The high incidence of peritoneal implants, we feel, adds to the hypothesis but hardly justifies a conclusion either for or against it.

Factors in favor of spread by way of lymphatic vessels, some of which have been mentioned previously by others, are (1) the high incidence of bilateral ovarian involvement; (2) the smooth surface of the involved ovary, adhesions rarely being encountered; (3) maintenance by the involved ovary of the shape of the normal ovary; (4) the widespread and extra-abdominal metastasis sometimes found; (5) the high incidence of peri-aortic lymph node involvement; (6) the demonstrable evidence of carcinomatous cells in the peritoneal lymphatic vessels; and (7) the occurrence of ovarian carcinoma secondary to carcinoma of the breast.

It is obvious that no strong argument can be advanced to support the

hypothesis that bilateral involvement is suggestive of spread by way of lymphatic vessels. The smooth surface and maintenance of normal ovarian shape certainly are suggestive of growth from within. The simplest entrance to the medulla is surely through the hilus by way of lymphatic vessels (Fig. 5). The widespread metastasis so often found outside the abdominal cavity necessitates spread either by lymphatic vessels or by the blood stream. It may be said that the peri-aortic nodal involvement, so often found, is secondary to the

FIG. 4.—Peritoneal lymphatic vessel loaded with carcinomatous cells. (×150)

FIG. 5.—Cortex of ovary, showing lymphatic vessel which contains carcinomatous cells. (×125)

ovarian lesion that previously had arisen by some other route. This may be true. Ovarian carcinoma secondary to carcinoma of the breast must start at least through the agency of the lymphatic or blood stream.

We believe that the above-mentioned reasons are suggestive of the likelihood of spread by way of the lymphatic vessels in many cases. As stated, this may not always be by retroperitoneal spread and in turn by retrograde spread, but may in some instances be by way of the peritoneal lymphatic vessels. Figure 6 represents a section of ovary that showed no gross evidence of metastatic lesions. By cutting several sections this tiny metastatic nodule was found. In contrast to Figure 2, showing a small nodule near the periphery, this metastatic nodule is near the medulla, adjacent to a lymphatic vessel.

Extension by continuity from structures adjacent to the ovary unquestionably does occur. Although little has been written regarding this type of spread, one may perhaps infer that it is conceded by all.

Extension by way of the blood stream certainly is within the realm of possibilities. This type of spread is sometimes used to explain metastasis from the breast to the ovary. There is no reason for thinking that blood vessels are not occasionally eroded giving rise to spread by way of the blood stream.

The only logical conclusion, with our present knowledge, is that metastasis may occur in any one or in all of the ways already mentioned. The predominant type of spread in any particular case probably depends on at least three factors: (1) The site of the primary lesion; (2) the depth to which the wall of the primarily involved viscus has been invaded; and (3) the degree or grade of malignancy of the primary lesion.

Does a primary adeno-"colloid" carcinoma of the ovary ever mimic Krukenberg's tumor? Primary adeno-"colloid" carcinoma of the ovary does

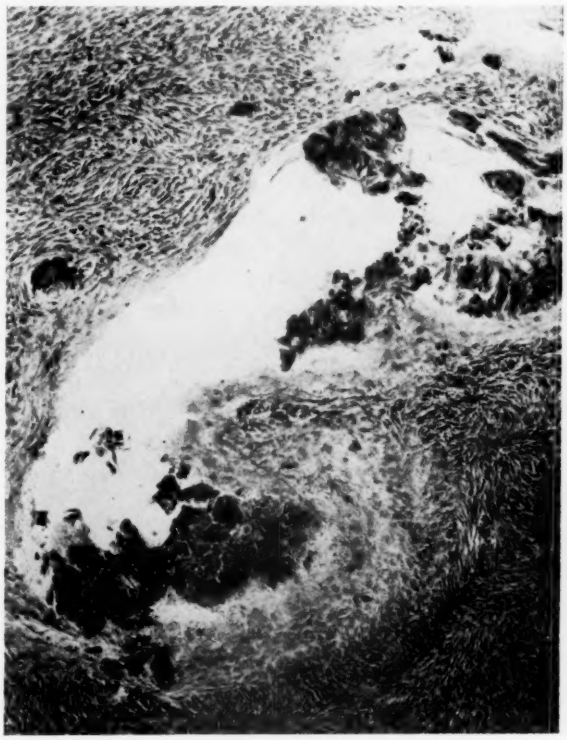

FIG. 6.—Hilus of ovary showing lymphatic vessel which contains carcinomatous cells. (×85)

occur. The case reported by Andrews[2] is the most convincing, but it may yet prove to be a metastatic lesion. It may be safely concluded that primary adeno-"colloid" carcinoma of the ovary may rarely mimic Krukenberg's tumor. At present, the most plausible explanation regarding the origin in the ovary is the hypothesis that an entodermic type of epithelium predominates and inhibits the other elements in an originally teratomatous lesion.

What surgical procedures are indicated in dealing with these cases? This, of course, depends on many factors, chief of which are the patient's general condition and the extent of the growth. Given a patient who is a poor surgical risk or one showing evidence of extensive metastasis, surgical treatment is

contraindicated, save for the relief of an obstruction of the gastro-intestinal tract. Given a patient who is a good surgical risk without extensive carcinomatosis, the uterus, tubes and ovaries should be removed. This procedure is justified for three reasons: (1) The pathologist's diagnosis may be wrong; (2) the remaining days or months which the patient has to live will be more comfortable without the presence of a huge pelvic mass and abundant ascites; (3) the increased mortality and morbidity associated with this procedure are not great enough to warrant not attempting to give the patient the comfort that would result from such a procedure. Circumstances may justify leaving the uterus intact but an apparently atrophic ovary should never be left intact. Two of our cases emphasize this point. In one, a unilateral, solid ovarian tumor was removed elsewhere. This patient registered at the clinic four months later and had a tumor of the remaining ovary with considerable ascites. In the second case, which was similar to the first, not even a palliative procedure was advised owing to the extensiveness of the gastric lesion, as shown on roentgenologic examination. Both patients could have been made comfortable longer with adequate original surgical treatment. We are aware that every surgeon cannot have a pathologist at his side, particularly one who is experienced with the diagnosis of fresh tissue. A good general rule, in this case, is to remove both ovaries when a solid tumor is found involving either one, particularly if the patient is past or near the menopause.

What surgical interference is warranted in dealing with the primary lesion? This, in our opinion, usually depends upon one factor—the site of the primary lesion. All things being equal, the surgeon is justified in being more radical when the primary lesion is in the colon than when it is elsewhere, because of the frequent relatively low grade of these lesions.

Are any other types of treatment indicated? Fennel[13] reported a case of intercurrent development of uterine carcinoma. Radium treatment for the uterine lesion was of benefit but the gastric carcinoma then seemed to become more active.

SUMMARY

We have presented 44 cases of Krukenberg's tumors, five of which previously have been studied and reported by Masson.[26] We believe that the term "Krukenberg's tumor" should not be used. However, since, in all probability, such a term will continue to be employed, all metastatic adenocarcinomata of the ovary should be included in this group. We have attempted to show that these tumors vary only in size and degree or grade of malignancy. We have demonstrated a few metastatic, "signet-ring," carcinomatous cells in the cortex of an ovary that need only time in order to invade the entire ovary and to produce a typical gross pathologic and clinical picture of Krukenberg's tumor. We have demonstrated the tremendous structural variation seen in different parts of the same microscopic section, as evidence of the wide variation in structure throughout the tumor. This, we feel, supports our contention that tumors found to contain glandular structures when examined

microscopically should not be excluded. We have further stated that nearly all Krukenberg's tumors will show some glandular structures if serial sections are made. In our experience, mucus has always been found, as evidenced by the presence of "signet-ring" cells. The variation in the amount of glandular structure and amount of mucus, we believe, is largely dependent on the grade of malignancy of the primary lesion, varying inversely.

That metastasis may occur in one or all of four ways is our contention. This conclusion is based on the following observations: We have found peritoneal lymphatic vessels loaded with carcinomatous cells; this observation demonstrates the possibility of spread through peritoneal lymphatic channels. Peritoneal implants may arise from similarly involved, adjacent lymphatic vessels. Spread to the ovary may occur by this route. The high incidence of involvement of peri-aortic nodes is suggestive to us, as it has been to others, of spread frequently by the retroperitoneal lymphatic system. It has been pointed out that there is no reason why carcinoma may not spread by way of the blood stream, when blood vessels are eroded by the growth. We do not doubt that spread may occur by infiltration of contiguous structures. Lastly, spread by a process of peritoneal sedimentation is, to us, perfectly logical. Carcinomatous cells are frequently found in peritoneal fluid in cases of carcinoma of the stomach. Spread by this route, therefore, is logical for there is no reason why the ovary should not be involved when the peritoneum is involved, as is indicated by the presence of peritoneal implants. If one admits the logic of this argument and believes that carcinoma may spread by way of the lymph stream, blood stream, and by infiltration of contiguous structures there can be only one conclusion. That conclusion is that spread may be by any one or by all four ways.

We have stated above that the predominant type of spread in any particular case probably depends on at least three factors: (1) The site of the primary lesion; (2) the depth to which the wall of the primarily involved viscus has been invaded; and (3) the degree or grade of malignancy of the primary lesion.

It is our belief that primary adeno-"colloid" carcinoma of the ovary rarely mimics Krukenberg's tumor. Infrequently it is difficult to distinguish between an edematous primary ovarian carcinoma and a metastatic "colloid" carcinoma of the ovary. The comparatively typical stromal reaction seen in an ovary being invaded by carcinoma and its value in helping one to distinguish between a primary and secondary ovarian carcinoma has been pointed out.

It is difficult to make general rules as regards treatment. As in cases of carcinoma occurring elsewhere in the body operation perhaps offers more than does any other type of treatment. We admit, however, that we do not actually know the value of other types of treatment, particularly roentgenotherapy. We bring up the question as to whether roentgenotherapy, in some instances, may hasten death. The tendency to be more radical in dealing with this condition when the primary lesion is in the colon has been suggested because of the frequent relatively low grade of these lesions. Although

the surgeon is confronted with a hopeless situation, he must not be blinded by the futility of trying to cure metastatic carcinoma but he must realize the value of palliation and of adding a few months to the patient's life.

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DESMOID TUMORS*

A CLINICAL AND PATHOLOGIC STUDY

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DESMOID TUMORS are benign fibromata arising from musculo-aponeurotic structures. According to MacCarty,[29] they are fibrocytomata occurring in striate muscle. The majority of them occur in the anterior abdominal wall, but they also occur, not infrequently, in other parts of the body.

This study is concerned with the clinical and pathologic manifestations of the 77 desmoid tumors which have been diagnosed at the Mayo Clinic during the past 30 years (January 1, 1908, to December 31, 1937, inclusive). The histories of these cases have been carefully abstracted, with especial reference to sex, age, symptoms, known duration of tumor, trauma, previous operations, pregnancies, treatment and recurrence, where definite follow-up information was available. The gross specimens were studied, and microscopic sections were made of each tumor in order to study cellular detail.

In order to be able to compare the results of this study with the results of those reported in the literature, desmoid tumors have been divided into two groups: (1) Those occurring in the anterior abdominal wall; and (2) those occurring in the musculo-aponeurotic structures elsewhere in the body.

The history of desmoid tumors apparently began in 1832, with the report of two cases by Macfarlene, of Glasgow. Although he did not coin the term "desmoid," there can be little doubt, from the details given, that the tumors were examples of fibroma of the abdominal wall. The first was described under the title, "Organized Sarcomatous Tumour between the Layers of the Abdominal Muscles," and the other as a "Fibrocartilaginous Tumour" in the same situation. The first patient was cured by excision of the tumor; the second patient died of peritonitis following excision of the tumor.

Müller, in 1838, first suggested the use of the term "desmoid" because of the band and tendon-like arrangement in these fibrous tumors. However, the tumors were called, and generally referred to by the French term *"fibrome de la paroi abdominale"* until Sänger (1884) revived the term "desmoid" in conjunction with his operative innovation of resecting the peritoneum in

* The material in this paper was submitted by one of us (Pearman) to the Faculty of the Graduate School of the University of Minnesota, in partial fulfillment of the requirements for the degree of M.S. in Surgery.

cases in which this membrane was adhered to the growth rather than shelling out the tumor from its false capsule as previously had been done.

According to Labbé and Remy, nine cases of desmoid tumors had been reported prior to 1850. The fibrous nature and benign character of these tumors were recognized from the onset, although there was much controversy as to their point of origin. Huguier (1860) correctly stated the fibrous nature of the growth, but believed that it arose by a pedicle from the periosteum of the pelvis, and suggested section of the pedicle as a method of treatment.

While the French were being misled by Huguier, Cornils (1865) and Buntzen (1868) developed the musculo-aponeurotic theory of origin and suggested treatment by excision. Guyon, in 1877, corrected the error initiated by Huguier. In 1875, Suadicani made the great advance of applying listerism to the extirpation of these tumors.

Except for occasional case reports, the term "desmoid" was seldom seen in the literature until 1890, when Ledderhose reviewed 100 cases reported in the literature, and, in 1904, when Pfeiffer, in a monograph, collected and analyzed 400 cases (40 of his own and 360 reported in the literature). Since then various case reports and summaries have appeared in the literature, such as those of Stone, Balfour, Stewart and Mouat, Bessesen, Bevan, Cullen, Delbet, Marlow, Polacco, Powers, Walters and Church, Nichols, Danforth, Cahn, Andrews, Mason, Penick, and Geschickter and Lewis.

Mankin collected, from the literature, reports of 629 cases of neoplasms of the anterior abdominal wall; in 423 of the cases the neoplasm was a fibroma and in 152 it was a fibrosarcoma.

Most of the reports have concerned desmoid tumors of the abdominal wall; however, in a number of cases of desmoid tumors, such as those reported by Bellanger, Cigolini, Salto, Auvray,[2, 3] Hoffmeister, Mason and Esau, the tumors occurred elsewhere in the musculo-aponeurotic structures of the body.

Desmoid tumors are of comparatively infrequent occurrence. Gurlt, of Vienna, found only eight in a study of 16,637 tumors. Labbé and Remy observed ten cases during 20 years; Billroth, 16 in 23 years; Nélaton, 15 in 26 years; Pfeiffer, 40 cases at von Brun's Clinic, at Tubingen, in 46 years, and Mason, 50 cases during 24 years.

Although the real cause of these tumors still remains unknown, much has been written on this phase of the subject.

In the 400 cases included in the monograph by Pfeiffer, 87.1 per cent of the patients were women. Data regarding the occurrence of pregnancy were available in 265 of the cases in which the patients were women. In 250, or 94.3 per cent of the 265 cases, the patients had borne children. In 93 per cent of the cases reported by Stewart and Mouat the patients were women, and 80 per cent of these women had borne one or more children. In most of the cases reported by Stewart and Mouat the tumor occurred in the third or fourth decade of life. Geschickter and Lewis reported 20 cases of desmoid tumors of the abdominal wall. In 19 of the cases the patients were females; in 17 of the 19 cases the patients were between the age of puberty and the

menopause. All of the tumors were related to pregnancy or the scar of an operation. These authors stated: "The rarity of such fibromata . . . is in keeping with the simple and direct formation of adult fibrous tissue from mesenchyme. The simplicity of this differentiation in a tissue which retains its power of regeneration supplies very few 'embryonic rests,' in the sense of Cohnheim, from which tumors might arise." These authors expressed the opinion that there is some relationship between these growths and sex physiology.

Stewart and Mouat said that there was a history of trauma or severe muscular strain in nine of their cases and that the tumor occurred in an operative scar in five cases. Penick, in a review of the literature, found reports of 15 cases in which the tumor arose in operative scars and added two cases in which this occurred. Auvray,[2] Esau, Hoffmeister, and Cigolini also reported trauma as a possible causal factor. Ebner, in 1880, advanced the theory now held by MacCarty,[26] namely, that these tumors result from muscular rupture either in consequence of violent effort or traumatism. Labbé and Remy (1888) suggested that muscular rupture during violent contractions of labor was the real explanation, that is, the physiologic trauma of labor.

In view of the traumatic theory, Nørgaard contrasted the comparatively common hematoma of the rectus muscle caused by severe strains or infectious diseases with the rare spontaneous hematoma in the same muscle. In all of the 72 cases which he reported, the patients were women, and all of the women except one were multiparae. In 11 cases spontaneous hematoma occurred during pregnancy. The clinical picture was usually misinterpreted and practically all of the patients were treated surgically.

It appears highly probable that this condition may be the basis of desmoid tumors, that is, organization in an hematoma and subsequent hyperplasia, the cause of the latter being unknown. Repetto expressed the opinion that a desmoid tumor is the result of an inflammatory reaction in a small hemorrhage in the abdominal wall followed by fibrosis and hyperplasia.

Various clinical observations have been reported in regard to these tumors. Stewart and Mouat said that the tumor is usually discovered accidentally by the patient or by a physician after some slight trauma has led to physical examination. The presence of the tumor may occasionally cause pain of a localized or radiating nature. Even when the tumor has attained considerable size it rarely causes pressure symptoms, and signs and symptoms of intra-abdominal involvement are lacking. The tumor does not involve the skin, which can be moved freely over the tumor. With the abdominal muscles relaxed, the tumor can be moved about in certain directions with sufficient freedom to show that it is unconnected with any intraperitoneal structure. It is also immobilized by contraction of the muscle or muscles in which it lies and recovers its mobility when the muscles are relaxed. It must be considered in the differential diagnosis of tumors occurring in operative scars, as pointed out by Balfour, Danforth and Mason. Cigolini, Salto, Auvray[2, 3] and Esau have pointed out that the tumor must be suspected in all cases in which a

tumor occurs in muscle and that a biopsy should be performed to determine its exact nature.

The gross and microscopic appearance has been well-described by various authors. Stewart and Mouat reported that the tumors always occur singly. They may be oval, round or flat, and they may vary in size from 1 to 12 cm. in diameter. Rokitansky (1880) described one weighing 17 Kg. Montgomery and Bland (1905) reported a case in which the tumor weighed 19 pounds (8.6 Kg.). The tumor may become adherent to the fascia or peritoneum. Owing to the pressure of the growing tumor against adjacent structures it may appear encapsulated. It is densely hard, white or pinkish, and cuts with difficulty.

The microscopic structure, according to Geschickter and Lewis, is that of a rather cellular fibroma occurring in striate muscle. The tumor is clearly an infiltrating type, without a capsule. The especial features of the tumor are the inclusion of striate muscle, as described by Durante (1902).

The treatment, according to most of the writers on the subject (Balfour, Mason, Stewart and Mouat, Pfeiffer, Penick, and Geschickter and Lewis), is surgical.

The prognosis, according to Geschickter and Lewis (1935), is good, as the majority of their patients lived well beyond the five-year period, after surgical removal of the tumor. Pfeiffer (1904) in a postoperative study of 107 cases found a recurrence in 33, or 30.8 per cent. In Stone's first case (1908) the tumor recurred and was again excised, 20 years after the first operation. In Morison and Drummond's case there was no evidence of recurrence two years after the second excision.

ANALYSIS OF CASES

An analysis of the present series of 77 cases of desmoid tumor reveals that in 55 cases the tumor occurred in the anterior abdominal wall, and in 22 cases it occurred elsewhere in the skeletal muscular system (Table I).

TABLE I

SITE OF DESMOID TUMORS

Site of Tumor	No. of Cases
Anterior abdominal wall (rectus abdominis, external or internal oblique, or transversalis muscles)	55
Pectoralis major	5
Muscles about the scapula	4
Rectus femoris	3
Gluteal muscles	2
Sternomastoid muscle	1
Posterior belly of digastric muscle	1
Biceps brachii	1
Extensor carpi ulnaris	1
Hamstring muscles (biceps femoris, semitendinosus and semimembranosus)	1
Dorsum of foot	1
Masseter	1
Scar of radical operation on the breast	1
Total	77

The following is an analysis of the 55 cases in which the tumors occurred in the anterior abdominal wall. In 40 cases, the patients were females, and in 15 cases, the patients were males. Most of the tumors occurred between the ages of 20 and 40, among the females, and between 40 and 60, among the males. The size of the tumors varied widely; in most cases the tumors were between 3 and 8 cm. in diameter. The known duration of the tumors varied from one month to several years. No relationship was noted between the size of the tumor and its known duration. There was a history of pregnancy in 25 of the 40 cases in which the patients were females. A history of trauma was obtained in four cases, and in 14 cases the desmoid tumor occurred in an operative scar. In 47 cases the patients were treated by excision, and in eight cases they were treated by a combination of excision and irradiation. Follow-up information was available in 47 of the cases in which the tumor occurred in the anterior abdominal wall. In 39 of the 47 cases excision only was employed, and in the remaining eight cases excision and subsequent irradiation were employed. Local recurrence of the tumor was noted in three cases in which the treatment consisted only of excision of the tumor, and in one case in which irradiation was employed following excision. In two of the three cases in which a local recurrence followed treatment by excision only, the recurrent tumors were excised, and follow-up data are available for eight and ten years, respectively, after the second operation. The tumor did not recur after the second operation in either case. In the 55 cases in which the tumors involved the anterior abdominal wall, 20 patients were known to be alive ten years, and 16 patients are known to be alive five years, respectively, following the completion of treatment. There were 20 known ten-year cures and 16 known five-year cures in this group of cases.

The following is an analysis of the 22 cases in which the tumor occurred elsewhere in the skeletal muscular system than in the anterior abdominal wall. The site of the tumors is shown in Table I. In the 22 cases, seven patients were males and 15 were females. Most of the tumors occurred between the ages of 20 and 40, in the females, and 40 and 60, in the males. The size of the tumors varied from 1 cm. to 10 cm. in diameter. The known duration of the tumors varied from one month to 24 years. No relationship was noted between the size and known duration of the tumor. There was a history of pregnancy in eight cases, and a history of trauma was obtained in two cases. The tumor occurred in an old operative scar in only one case (Table II). In 16 cases, the patients were treated by excision only, and in six cases, the patients were treated by excision combined with irradiation therapy. Follow-up information was available in 15 cases. In ten of the 15 cases, treatment consisted of excision only; in the remaining five cases, excision was followed by irradiation. There was a local recurrence of the tumor in the ten cases in which excision only was employed, but no local recurrence was observed in the five cases in which excision was followed by irradiation. In the 22 cases, in which the tumors were situated elsewhere than in the anterior abdominal wall, three of the patients have lived for ten years, and four patients

have lived for five years, respectively, following the completion of treatment (Table II).

TABLE II

CLINICAL DATA AND RESULTS OF TREATMENT IN 77 CASES OF DESMOID TUMOR

	Sex					Treatment		Results					
								Patients Known to have Lived 10 Years Following Treatment		Patients Known to have Lived 5 Years Following Treatment		Recurrence of Tumor	
Site of Tumor	Males	Females	History of Pregnancy	History of Trauma	Tumors Occurred in Operative Scar	Excision Only	Excision and Irradiation	In Cases in which Excision Only was Employed	In Cases in which Excision and Irradiation were Employed	In Cases in which Excision Only was Employed	In Cases in which Excision and Irradiation were Employed	In Cases in which Excision Only was Employed	In Cases in which Excision and Irradiation were Employed
Anterior abdominal wall	15	40	25	4	14	47	8	18	2	12	4	3*	1
Other parts of body	7	15	8	2	1	16	6	1	2	2	2	3	
Total	22	55	33	6	15	63	14	19	4	14	6	6	1

* In two of these cases the recurrent tumor was excised; in the two cases there was no evidence of a second recurrence eight and 12 years, respectively, after the second excision.

The following is an analysis of the 77 cases. Twenty-two of the patients were males and 55 were females. A history of pregnancy was obtained in 33 cases, a history of trauma was obtained in six cases, and the tumor occurred in an operative scar in 15 cases. In 63 cases, treatment consisted of excision only; in the remaining 14 cases, excision was followed by irradiation. There was a local recurrence of the tumor in six, or 9.5 per cent, of the 63 cases in which excision only was employed, and in one, or 7.1 per cent, of the 14 cases in which excision was followed by irradiation. There were 23 known ten-year cures and 20 known five-year cures.

There was only one postoperative death in the entire series of 77 cases. This was due to infection of the operative incision following the removal of a large desmoid tumor from the anterior abdominal wall (an operative mortality of 1.3 per cent).

CLINICAL ASPECTS

Desmoid tumors must be considered in the differential diagnosis of all masses that are situated in or come in contact with the musculo-aponeurotic structures of the body. In this series of cases the patients, generally, sought aid because of the presence of a tumor mass. Other less frequent complaints were: A dragging sensation or sense of weight in the abdomen; a mild sticking pain; a sudden increase in size of a previously small nodule; a bizarre pain in the abdomen; and a sense of pressure on the bladder.

In this series of cases the desmoid tumors were found more frequently in the anterior abdominal wall than elsewhere in the body and, occasionally, had

been diagnosed by the clinician as being intra-abdominal. They had been mistaken for hydrops of the gallbladder; a large stone in the gallbladder; a tumor of the omentum or mesentery; pancreatic cyst; a uterine tumor, a tumor of bone; and a tumor of kidney. When situated elsewhere in the body they generally had been mistaken for sarcomata.

The following points have proved of value in the clinical diagnosis of these tumors. As a rule the tumor is smooth, round or flat, firm and discrete. The tumor is situated below the skin but is not attached to it. The tumor is movable, moves with the muscle to which it is attached, and is immobilized by contraction of this muscle. On deep inspiration the tumor moves forward but not downward as do most intra-abdominal tumors.

A desmoid tumor must be distinguished from keloids, fibrosarcomata, inflammatory conditions, and lesions which extend secondarily to the abdominal wall from nearby organs. A keloid will, more frequently, be difficult to distinguish from a desmoid tumor than will other conditions mentioned because this overgrowth of fibrous tissue is closely allied to the desmoid tumor and resembles it in many respects. The common keloid involves the skin and subcutaneous tissues to form raised regions covered with shiny epithelium; in this respect it differs from a desmoid tumor, which involves the skin occasionally, and then only secondarily, and is usually situated below the skin. These two conditions can also be differentiated microscopically. The keloid is relatively acellular with conspicuous tracts of collagen; the remains of obliterated capillaries are usually visible. A desmoid tumor is more vascular and more cellular than a keloid and evidences of cellular activity are more noticeable.

According to MacCarty,[27, 28] the only way to be certain of the diagnosis is to remove a specimen at the time of operation and examine it microscopically.

GROSS AND MICROSCOPIC PATHOLOGY

A freshly removed tumor is dense, hard and tough, and creaks under the knife. The cut surface bulges, is white or pinkish in color, glistens, and the interlacing bundles of white fibrous tissue are usually seen without difficulty (Fig. 1). The larger tumors tend to be soft in the center, either from edema or mucoid degeneration, and some are cystic. Changes in the skin covering the tumor are unusual. There was no associated involvement of the lymph nodes in this series of cases.

The histologic picture is that of a rather cellular fibroma occurring in striate muscle. The central portion of the tumor proved to be older than the peripheral portion. The elongated adult fibrous tissue cells run in strands and bundles which are interlaced in all directions after the manner of the unstriate muscle bundles in a uterine fibroid (Figs. 2 and 3).

At the periphery, where the tumor infiltrates the surrounding muscle, there is a tendency for the tumor to be somewhat more cellular. There is no capsule or definite line of cleavage between the tumor and the adjacent muscle. It is only when the tumor is bounded by a fascial plane that the appearance of

encapsulation is produced (Fig. 4). In spite of this infiltration there was no evidence of a sarcomatous change, such as nuclei containing large amounts of darkly-stained chromatin or large multiple nucleoli, both of which are indications of rapid proliferation. Normal adult blood vessels were noted throughout most of the tumors. These vessels were an indication of the slow growth of the tumor.

FIG. 1.

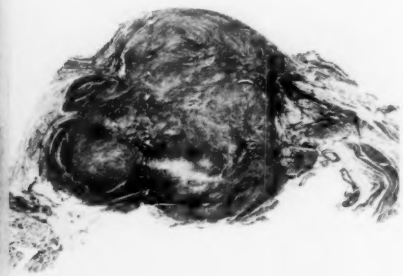
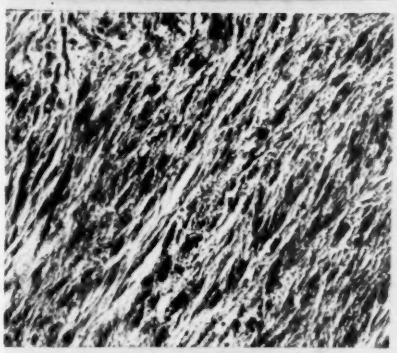


FIG. 4.

FIG. 2.



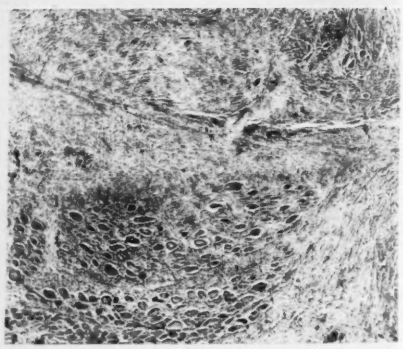
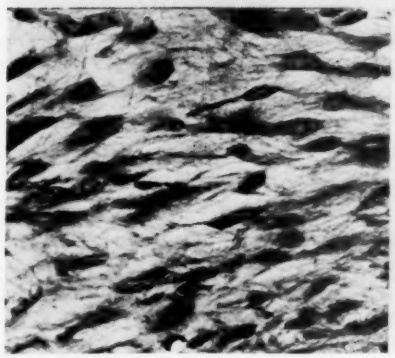


FIG. 5.

FIG. 3.



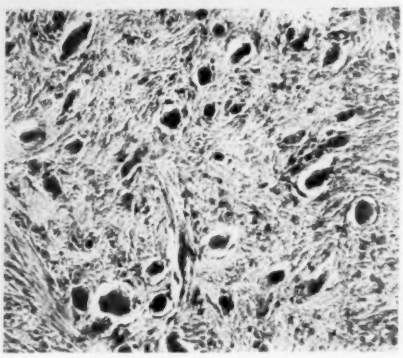


FIG. 6.

FIG. 1.—Desmoid tumor removed from abdominal wall, showing the characteristic band-like arrangement.
FIG. 2.—Cellular character of desmoid tumor. (×285)
FIG. 3.—Cellular but benign appearance of a desmoid tumor. (×450)
FIG. 4.—Cross-section of tumor lying between separated fibers of the rectus abdominis muscle in the rectus sheath; the tumor appears to be encapsulated. (×1¾)
FIG. 5.—Infiltration of muscle fibers by a desmoid tumor. (×30)
FIG. 6.—Muscle with "foreign body-like" giant cells. (×195)

The special features of the tumor were the inclusion of striate muscle fibers and the sequence of regressive changes. The earliest change was seen at the periphery of the tumor where the striate muscle was being infiltrated and broken up into constituent fibers (Fig. 5).

The muscle fibers appeared to be stretched and attenuated. They were irregular in outline and the transverse striations tended to disappear. Here and there were strands resembling unstriate muscle and "foreign body-like" giant cells derived from this muscle probably because of faulty nutrition (Fig. 6).

It is easy to see that failure on the part of the surgeon to remove the tumor completely would leave strands of interfibrillar desmoid tissue and result in a local recurrence of the tumor.

COMMENT.—The cause of these tumors as yet remains unknown. However, the most logical theory of origin seems to be one of trauma superimposed on individual predisposition. A history of trauma was obtained in 21 cases (accidental trauma in six cases and operative trauma in 15 cases), and a history of pregnancy (physiologic trauma of labor) was obtained in 25 cases. Thus trauma appeared to be an etiologic factor in 46, or 60 per cent, of the cases studied. The endocrine theory, as related to pregnancy, seems void because 22 patients were males and only 33 of the 55 females had been pregnant.

No differences in etiology, clinical findings, pathology, curative treatment, or prognosis could be noted between the tumors which occurred in the anterior abdominal wall and those which occurred in other parts of the body.

At first glance, it would appear that a combination of excision and roentgenotherapy would be the ideal treatment, since there was a recurrence in 9.5 per cent of the cases in which the patients were treated by excision only, and in only one, or 7.1 per cent, of the cases in which the patients were treated by a combination of roentgenotherapy and excision. However, several factors have to be considered: (1) The small number of cases in which the patients were treated by excision and radiation (14) as compared to the number treated by excision only (63), (Table II); (2) the insignificance of the difference in number of five-year and ten-year cures obtained by the two methods (Table II); (3) no definite criteria were used for the employment of roentgenotherapy—it was employed in some cases in which the tumor was completely removed surgically but was not used in some cases in which the tumor was large or difficult to remove; and (4) a few of the patients had been treated unsuccessfully by roentgenotherapy only before they finally were cured by surgical treatment.

SUMMARY

This paper is based on a study of 77 cases of desmoid tumors. In 55 cases the tumor occurred in the striate muscle of the anterior abdominal wall, and in the other 22 cases it occurred in striate muscle elsewhere in the body. A desmoid tumor is a simple fibrous tumor that arises in musculo-aponeurotic

structures and tends to infiltrate the muscle in which it lies. Trauma (accidental, operative, or the physiologic trauma of labor) combined with an unknown individual predisposing factor, appears to be the most logical theory of origin. There was a peculiar change in the striate muscle fibers enclosed in the growth. This change appears to be a process of differentiation and results in the formation of multinucleated plasmodial masses resembling foreign body giant cells. These tumors do not undergo metastasis nor do they endanger life; however, they do tend to recur locally, unless completely removed. Diagnosis is made by finding a fibrous tumor in muscle; the tumor is fixed by contraction of that muscle. A biopsy is indispensable for diagnosis. Treatment consists of complete excision. Roentgenotherapy appears to be of little, if any, additional value. The operative mortality in this series of cases was 1.3 per cent. There was a local recurrence of the tumor in seven, or 11.8 per cent, of the 69 cases in which follow-up data were available. We did not discover any evidence that this tumor ever undergoes sarcomatous change.

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TECHNIC OF TATTOOING WITH MERCURY SULFIDE FOR PRURITUS ANI

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IN A BRIEF REVIEW of the history of tattooing employed in surgery, Shie[1] stated that, in 1835, Pauli had successfully employed tattooing with mercury sulfide and white lead for the restoration of the natural color to the skin in cases of *nevus maternus* and superficial *nevus vascularis*; that Schule, in 1850, had recommended cosmetic tattooing with mercury sulfide following plastic operations upon the lips, and that the natives of Africa had incorporated powdered carbon in the wounds of other parts of the body so that the healed scar would be black to match the color of their skin. Carton,[2] in 1909, described the use of tattooing by the native savages of North Africa for the treatment of a variety of other lesions including the neuralgias. The association of tattooing therapy with neural lesions has more than passing significance. Dohi,[3] in 1909, noted that syphilitic cutaneous lesions do not appear in the areas tattooed with mercury sulfide. Dohi's observations had been confirmed by Aoki[4] and Belote.[5] On the basis of these observations, Cattani,[6] in 1922, recommended therapeutic tattooing with mercury sulfide (and other drugs usually employed topically) for the treatment of chronic, localized cutaneous lesions. In 1938, Hollander[7] reported his studies on tattooing with mercury sulfide for the successful treatment of intractable pruritus ani.

While a critical attitude toward a newly proposed treatment for pruritus ani is justified (since over 200 different forms of treatment are said to have been proposed[8]), the distressing character of the lesion warrants the trial of new procedures. It is with such an attitude that we approached the investigation of the treatment of pruritus ani by tattooing with mercury sulfide. For this study, 22 patients with intractable pruritus ani of long standing, who had failed to respond to established therapeutic measures, were accepted for tattooing with mercury sulfide. The results obtained in this group of patients was so satisfactory as to encourage the continuation of tattooing with mercury sulfide as a therapeutic procedure.[9] On the basis of subsequent experience, one of us (R. T.) has extended this form of treatment to a wider variety of cases.[10, 11]

The mechanism of the action of mercury sulfide deposited in the corium by tattoo is still undetermined. Our control studies showed that the me-

chanical trauma, alone, as produced by the tattooing machine without the employment of mercury sulfide is ineffectual in controlling pruritus ani permanently.[9] The present investigations suggest that a pharmacodynamic degenerative effect upon the cutaneous terminal nerve supply is produced which alters the capacity of the terminal nerve network to respond to adequate stimuli.[10] It is, also, likely that the alteration in the cutaneous modalities is proportional, within limits, to the amount of the intracutaneous deposit of mercury sulfide.[10, 12] These problems are new and are receiving further study.

Cattani[6] felt that mercury sulfide deposited in the corium may act as an antiseptic. However, convincing proof for this contention is still lacking. Dohi,[3] long ago, questioned the value of mercury sulfide in infections other than syphilis.

The studies of the effect of the intracutaneous deposit of mercury sulfide by tattoo upon the activity of the cells of the reticulo-endothelial system (which are present in abundance in the corium) are being pursued.

In this communication the technic of therapeutic tattooing of the anal canal and perianal circumference will be described in detail. Since the adoption of this technic the incidence of "skipped" areas (where localized areas of pruritus may continue, and which is erroneously regarded as a recurrence of pruritus) has been greatly eliminated.

Surgical Anatomy of the Anal Canal.—Embryologically, the anal canal begins at the pectinate line or the level of the papillae and crypts of Morgagni. For practical purposes[13] the starting point of the anal canal can be considered as the level at which the rectum passes through the pelvic diaphragm, *i.e.*, where the so-called fibromuscular anorectal ring is formed by the internal sphincter, the deepest portion of the external sphincter, the puborectalis portion of the levator ani muscle, and by the longitudinal muscles of the rectum. The epithelium above the pectinate line is cuboidal and columnar in type. The epithelium of the anal canal between the pectinate line and the anal intermuscular septum (the point of attachment of the longitudinal muscle of the rectum to the lining of the anal canal between the lower border of the internal sphincter and the upper border of the subcutaneous portion of the external sphincter muscle) is firmly adherent to the underlying tissues, and consists of a modified squamous epithelium possessing no sweat and sebaceous glands, nor hair follicles. Below the level of the anal intermuscular septum, there is true skin which covers the anal and inferior aspects of the subcutaneous component of the external sphincter muscle. In pruritus ani, variable portions of the modified skin of the anal canal and of the true skin of the perianal circumference are involved.

The sensory nerve supply of the lining of the anal canal is primarily derived from the filaments of the inferior hemorrhoidal nerve.

General Procedure.—Systemic and general dermatologic disease having local anal and perianal representation are always appropriately treated and eliminated, if possible, prior to tattooing. When, however, the underlying

disease cannot be identified and successfully eliminated, one is forced to treat the symptom.

Women with pruritis ani and perinei, which occurs at or past menopause, are given a trial of estrogenic therapy (the equivalent of 150,000 to 250,000 rat units of estradiol benzoate* (Progynon B) administered in biweekly, intramuscular doses of 10,000 R.U.). If the localized pruritus is unrelieved following endocrine therapy, tattooing with mercury sulfide is carried out.

Prior to tattooing, the patient is patch-tested for evidence of cutaneous sensitivity to mercury, using 2 to 5 per cent ammoniated mercury ointment. Positive reactors should not be tattooed with mercury or its derivatives.

Tattooing with mercury sulfide or other chemicals is never carried out in the presence of inflammatory and infectious disease of the preformed anal ducts, anal glands, and the crypts of Morgagni. Lesions such as anal ulcers, hypertrophied papillae, suppurations, fistulae, and hemorrhoids, which are the result of infection of the previously mentioned anal structures, are always eradicated prior to tattooing. Redundant perianal skin, even in the absence of anal lesions, is excised to facilitate tattooing.

Operation and tattooing are never performed at one sitting because the primary operation may be adequate for the control of pruritus. Secondly, in the presence of open wounds, the mercury sulfide may get into the subcutaneous tissues and form mercury proteinate, which is toxic.

Armamentarium.—The armamentarium consists of an electric tattooing machine,† such as that used for ornamental tattooing, with needle handles containing eight to 20 needles in a single row (in a tubular metal sheath), and protruding for 2 to 4 mm. from the end of the sheath. The tubular sheath is adjusted so that when the machine is at a standstill the needle points are flush with the end of the sheath.

During tattooing, the needles have an up-and-down movement (the amplitude of which is 2 to 4 mm.) and a speed of about 3,000 vibrations per minute. A technical knowledge of the component parts of the machine, such as the terminals, the switchboard, the footswitch, and the rheostat is essential, and can be mastered best by actual contact with the equipment. The needle handles and the sheath are sterilized by boiling in water or preferably by formaldehyde vapor.

Technic.—The therapeutic tattooing of the anal and perianal regions requires from 45 to 60 minutes and is preferably undertaken in a hospital. In most cases, satisfactory tattooing is accomplished in one sitting.

The choice of an anesthetic depends on personal experience and preference. Any form of anesthesia that will last for an hour or longer is satisfactory. From a practical standpoint, the oil-soluble anesthetics (which alone have been employed for the treatment of certain cases of pruritus ani)

* Supplied by Dr. W. H. Stoner, The Schering Corporation.

† Recently, one of us (R.T.) has developed a simple, reciprocating, pneumatic tattooing pistol which has many advantages over the instruments employed previously.

are desirable. However, in order to permit a critical evaluation of the therapeutic tattooing alone, we have purposely refrained from using the long-acting oil-soluble local anesthetics because their inclusion would be equivalent to employing two forms of therapy.

The field to be tattooed is prepared as for any other anorectal surgical procedure. For practical reasons alcohol and ether are used rather than colored skin antiseptics. Following alcohol-ether preparation, it is customary to rub phenolized petrolatum into the skin which is to be tattooed.

The mercury sulfide is made into a moderately thick paste by mixing it with sterile distilled water. The end of the tubular sheath of the tattooing machine is either dipped into the paste or part of the paste is deposited in a specially constructed tip. The vibrations of the machine cause the paste to escape slowly to the points of the needles and thus the medication is deposited intracutaneously.

The tubular sheath of the machine should be held at an angle of about 40° to the skin. The skin should be held taut to obliterate the anal and perianal folds and to facilitate the penetration of the needles and the chemical into the corium. An area of skin, one centimeter long, the width of which varies with the number of needles used, is tattooed at a time. A slow,* steady, forward and backward or rotary motion of the instrument with light pressure against the skin is employed. This maneuver is repeated several times in the same area until the skin shows a uniform and permanent red stain which is evidence that a sufficient supply of mercury sulfide has been deposited in the corium. Adjacent skin is similarly treated until the entire pruritic region is tattooed.

The skin of the anal canal is treated first. Tattooing is begun at the anal verge and is carried cephalad to the pectinate line, using the needle handles containing 15 to 20 needles. The perianal skin is then tattooed radially to the anal orifice, beginning about one centimeter beyond the natural line of demarcation of the area of pruritus, which is discernible in the majority of cases. In the absence of such natural demarcation, it is desirable to delineate the extent of the involved perianal skin before the anesthetic is administered.

During the process of tattooing some of the paste of mercury sulfide escapes from the instrument and stains the untreated skin. It is essential to eliminate this excess paste by frequent wiping of the treated and untreated skin with gauze in order to avoid missing small areas of skin where localized areas of pruritus may continue. By tattooing the anal canal before the perianal region, staining of the lining of the anal canal with red mercury sulfide coming from the perianal circumference has been avoided. In spite of these measures, it is at times impossible to avoid skipping small areas of involved skin. These can, however, be dealt with easily at a subsequent time, if necessary.

* The speed of tattooing has been increased considerably with the use of the new pneumatic pistol.

After the completion of the tattooing, the treated area is covered with either phenolized petrolatum or with an ointment containing an anesthetic, such as ethyl aminobenzoate, metycaine or pontocaine. Edema and tenderness may occur and persist for 24 to 48 hours or longer, and are relieved by the application of anesthetic ointments, witch hazel dressings, hot compresses or by hot hip baths.

Desquamation of the tattooed epidermis ensues within a few days and reepithelization usually takes place in a few weeks after tattooing. Therefore, the mercury sulfide, to be effective, must be deposited in the corium. Deleterious effects or a foreign body giant cell reaction (commonly seen after the intracutaneous introduction of other foreign bodies) have not been observed in a comprehensive clinical and histologic study of skin tattooed with mercury sulfide.[12]

SUMMARY

A detailed description of the technic of tattooing with mercury sulfide for the treatment of intractable pruritus ani is presented.

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VARICOSE VEINS

AN ANALYSIS OF THE RESULTS OF VARIOUS OPERATIVE PROCEDURES

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DURING recent years there has been an increased interest in the treatment of varicose veins. This is evidenced by the number of publications on the subject as well as by the diversity of suggested methods of attacking this problem. However, very little that is new, either as regards treatment or mechanism of the disturbance has been brought forth.

In reviewing the many papers on varicose veins, we fail to find satisfactory follow-up studies of the patients treated, which makes it difficult to arrive at a comparison of end-results. Most writers have stressed one or another form of treatment without giving the end-results of their therapy. In no instance have we found the end-results compared, when various methods of treatment have been employed in the same clinic.

It is our purpose to present an analysis of the results of operative procedures in 121 patients cared for in the Varicose Vein Clinic of the New York Hospital, during the six years from 1932 to 1938.

Ochsner and Mahorner[1] have recently given an excellent and detailed account of the history of the treatment of varicose veins; therefore, no reference will be made to historical data here.

The forms of treatment of varicose veins most commonly employed at present are the following:

Injection.—At present, the most popular treatment of varicose veins is the injection of various sclerosing substances, of which sodium morrhuate is probably the most widely employed. Recurrences following injection are reported variously from zero to 98 per cent. Steubner,[2] in reporting 104 cases with 158 extremities completely treated by injection, was able to state that there had been no recurrences during a 15-month period. It is not stated how long the patients were followed after treatment. DeTakats[3] reports 10.6 per cent recurrences in 389 cases injected, but fails to tell the length of the follow-up studies. Howard, Jackson and Mahon,[4] however, report 98 per cent recurrences in 49 patients one year or more after treatment. They stress recanalization as a natural response to thrombosis and rightly state that treatment by injection—unaided by ligature, excision or stripping of main venous channels and perforating veins—will not assure a permanent cure in cases of varicose veins, except in a few isolated cases of dilated single veins with competent saphenous and perforating veins.

Simple Ligation.—Trendelenburg[5] advocated ligation of the varicose veins in the midthigh, and his results have been presented by Perthes,[6] showing 22 per cent recurrences in from five months to nine years. Although subsequent authorities are in agreement that this is a poor procedure and gives rise to a high incidence of recurrences, it is carried out in a large number of cases. DeTakats[3] reports 50 cases in which ligation was performed below the proximal competent vein. There is no mention made of tying off collateral vessels. No deaths followed this procedure, but three infected wounds are reported. While the follow-up on these patients is vague, all were said to be free from recurrences if the operative indications were correct.

Simple High Ligation.—High ligation preliminary to injection of sclerosing solutions has been employed extensively, many preferring to use it as an ambulatory treatment. Fergusson[7] reports 226 ligations upon 178 patients, with no deaths, and three infected wounds. The site of ligation is not clearly indicated but probably was high. His three- and four-year results include 37 operations upon 26 patients, with no relief of symptoms in two, venous stasis in six, and enlarged veins in 14. Eight of the patients with enlarged veins have no symptoms. In the classification employed in our follow-up, 14, or 35 per cent, of these results would be considered poor.

DeTakats and Quillen have carried out 200 ambulatory operations and stress the value of high ligation. The absence of pulmonary emboli is particularly noted, whereas little attention is given to hemorrhage, hematoma, infection of the wound with formation of an abscess, of an infection with death from septicemia, and reaction to procain which are present in the list of complications recorded. No injection was made at the time of operation because the majority of patients developed thrombosis without injection. Of the 200 cases, only 60 private patients were followed, and the length of the follow-up is not mentioned in these save in one followed for four years. They report dilatation proximal to the ligation in five, and distal to it in two cases.

Edwards[8] reviews the anatomic factors in high ligation of the saphenous vein, and recommends this procedure followed by injection, but he reports no follow-up studies.

High Ligation and Injection.—In the group of cases treated by high ligation and injection, follow-up studies are given with greater frequency than in the preceding methods. Lowenburg[9] used this treatment in 49 instances and reported 89 per cent cures, 4 per cent with fair results, and 7 per cent with recurrences. The length of the follow-up in his cases is not stated. Faxon and Barrow[10] have used high ligation and injection as an adjunct to injection alone in 1,072 extremities. Their end-results are based upon 365 operations performed upon 228 patients followed from 18 months to five years, with an average follow-up of 2.9 years. They record perfect results in 55 per cent, or 200 extremities; this estimate of results is made upon complete relief of symptoms and absence of tension in any of the veins left. Satisfactory results were present in 25 per cent, or 90 extremities. In this group are patients who are symptomless but have definite varicose veins.

The authors classify 20 per cent, or 75 extremities, as failures. In these patients the veins are again present with stagnation of blood in the superficial system. The presence of a recurrent ulcer placed the results in a category of failures. Retrograde injection of the distal segment in 90 per cent of the cases at the time of operation made no difference in the final rating. As complications, they list infected wounds in 2 per cent of their patients, and three cases of pulmonary emboli, of which two were fatal. In one case the femoral vein was ligated and injected by mistake. Their failures are attributed to faulty technic. In 29 extremities a high ligation was not performed, and in 35 extremities incompetent communicating veins were present.

Howard,[11] in 91 ligations and injections, was able to examine 78 a year or more after treatment. He demonstrated recanalization in 100 per cent but considered 77 per cent cured, as they had no visible dilated veins; in 15 per cent, the symptoms remained or recurred. The complications include hemorrhage in one case followed by a pulmonary embolus. These cases were followed from one year to 29 months.

High Ligation and Excision.—Linton,[12] in 50 cases, has divided the perforators beneath the fascia of the lower leg in addition to a high ligation, but he mentions no follow-up on his cases. This procedure presents the same problem as the older extensive operations of Madelung and others.

Analysis of the New York Hospital Series.—Since September 1932, 169 patients have been admitted to the New York Hospital and operated upon for varicose veins. Of this number, 121 cases have been followed for from one to six years after operation. Of the remaining 48, 20 are being followed but the operation was performed less than one year ago, while 22 have been lost to the Follow-Up Department. Reports on two patients were received through their family physician, and two reported by letter; these four are not included in the total analysis because they have not been examined in this clinic. Therefore, in this report 87 per cent of the patients operated upon have been followed, while 15 per cent have been lost to the Surgical Follow-Up Department.

There were two deaths from pulmonary emboli.

In the group of 121 patients, followed from one to six years, 178 extremities were operated upon, and our follow-up studies will be based upon this figure; for it represents a truer picture to refer to separate extremities than to individuals in whom a bilateral operation was performed.

Clinical Aspects.—Although most writers, including Ochsner and Mahorner, find varicose veins more frequent in women than in men, the incidence in this series of cases is almost evenly divided between the two sexes as there were 63 males and 58 females. As a rule, there was no predilection for either the right or left extremity; a fact noted by Steubner, in his 104 cases in which both lower extremities were involved in 52 per cent, the right in 25 per cent and the left in 25 per cent of the cases. In our series, 96 (54 per cent) operations were performed on the left leg and 82 (46 per cent) on the right leg. There is an anatomic factor which might explain the slightly

greater incidence of varicosities in the left leg, namely, the iliac vein has to pass posteriorly to the right iliac artery and may, as a consequence, suffer more back pressure.

The occupations in which the patients had been engaged varied, corresponding to general types of work performed by the clientele of the hospital as a whole. They included:

Housewife	43	Business man	9
Domestic servant (male and female)	20	Factory worker	6
Counterman (butcher, baker, grocer)	11	Miscellaneous	20
Laborer	12		
			121

The ages ranged from 22 to 77, and were distributed as follows:

20–30	10	41–50	38	61–70	7
31–40	38	51–60	26	71 and over	2
					121

All patients were first seen in the Varicose Vein Clinic and then recommended for admission to the hospital because they were not suitable for injection treatment. If the varicose veins were associated with ulcer, the latter condition usually was healed first by bed rest, elastoplast bandage, Unna paste boot, or injection before admission. In a few instances, patients with ulcer were admitted and treated for it prior to operation. We feel that an ulcer can be healed and that every effort should be made to do so before operation.

In addition to the usual history and physical examination, and by far the most important preoperative step in this group, is a careful examination of the varicosities by someone familiar with the anatomy and pathologic physiology of varicose veins. The importance of determining a previous thrombophlebitis and early history of cardiac disease cannot be emphasized too strongly. It is only by the painstaking performance of all examinations that poor results may be eliminated.

The tests which are found most helpful in determining the extent of the disease are the Schwartz test, Trendelenburg test, Perthe's test and the comparative tourniquet of Ochsner and Mahorner.

The anatomy of the superficial veins of the lower leg has been carefully reviewed by Edwards[8] and others. This venous system comprises the internal and lesser saphenous veins which communicate throughout with each other and, by communicating or perforating veins, with the deep circulation. The lesser saphenous vein empties into the popliteal vein in the popliteal fossa, while the internal saphenous, after receiving a group of superficial veins, meets the femoral vein at the fossa ovalis (Fig. 1). The importance of this group of veins is stressed repeatedly.

Operative Procedures.—In the series of cases at the New York Hospital, six different operative procedures have been carried out:

(1) *Simple High Ligation.*—Under local anesthesia, a 7 cm. incision is

made parallel to and 2 cm. below Poupart's ligament. The midpoint of this incision is placed 2 cm. medial to the femoral artery, which is identified by palpation. As the incision is deepened through subcutaneous tissues and fascia, a careful watch is kept for a bluish tint through the translucent fat, which indicates the proximity of the saphenous vein. This vein lies more medially, and is usually larger than one anticipates. In case the internal saphenous is not sighted, dissection of one of the tributaries will bring the operator upon the vessel. Dissection is facilitated by dividing the vein, one end of which is carried upwards—care being taken to keep within the fibrous sheath encircling the vein.

FIG. 1.—Showing the normal anatomy of the internal saphenous vein and its tributaries.

As the proximal end of the vein is exposed all branches are carefully divided and ligated; including the external pudendal, the external superficial femoral, the superficial circumflex iliac, the thoraco-epigastric and the superficial epigastric. These may enter singly into the internal saphenous, or in different combinations. They may even enter the femoral. The important point is that the femoral vein be visualized and exposed sufficiently to permit the accurate placement of a clamp and suture-ligature on the saphenous above the clamp. Another tie is now placed above the suture-ligature to prevent blood from coming in contact with the suture or injured intima. This tie is placed flush with the wall of the femoral vein but without encroachment upon its lumen (Fig. 2). No stump should be left. A segment of vein, some 12 cm. in length, is removed by continuing the dissection of the lower stump and ligating it. Closure of the wound is carried out in layers, black silk being employed throughout. An Ace bandage is applied and the patient gotten out of bed the day of operation. He is encouraged to walk about, but is not allowed to sit with the leg in a dependent position.

(2) *Simple High Ligation and Injection.*—This is carried out as described above, save that after transfixing the distal stump, but before tying the knot, sclerosing fluid is injected into the lumen of the vein.

(3) *High Ligation with Excision.*—A high ligation is performed, as described, and, in addition, other segments of the varicose veins are excised. In certain instances, this included the internal saphenous vein above the knee and, in a few cases, veins were excised both above and below the knee. These patients were kept in bed for a period varying from three days to two weeks before they were allowed to get up. Both deaths occurred in this group due to massive pulmonary emboli.

(4) *High Ligation and Low Ligation.*—This procedure has been mentioned very seldom, but would appear to offer excellent possibilities, and avoids the difficulties and dangers of more extensive operations. It consists

of the simple high ligation with the addition of a simple ligation of the internal saphenous below an incompetent perforator, usually above the level of the knee. Recently, we have employed this procedure with the injection of a

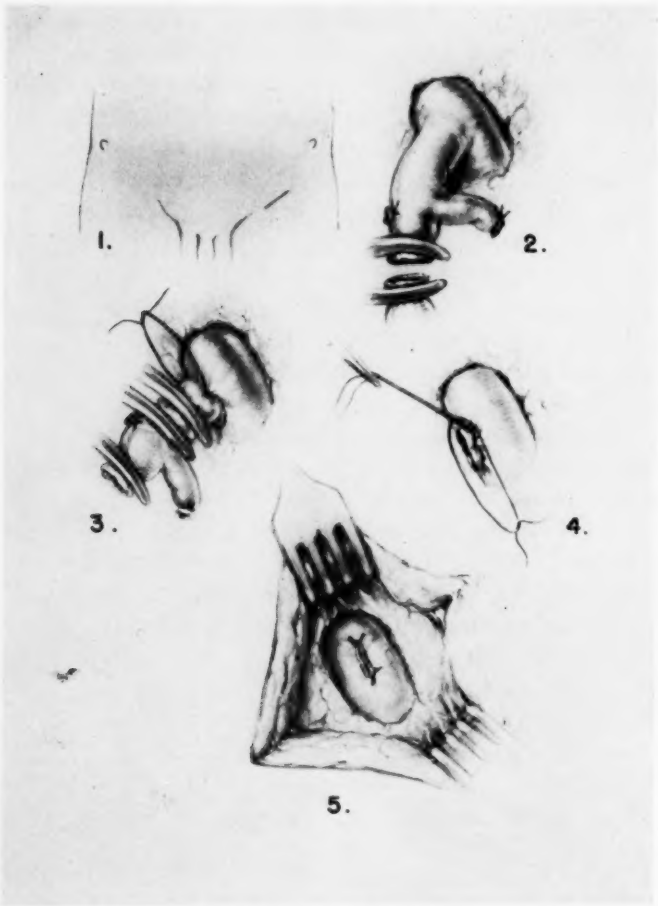

FIG. 2.—SIMPLE HIGH LIGATION OF THE INTERNAL SAPHENOUS VEIN:
(1) The incision is placed parallel to, and below, Poupart's ligament, over the femoral vein.
(2) The vein is isolated and divided between clamps to facilitate dissection of the upper stump. All branches are carefully divided and ligated.
(3) When the saphenofemoral junction is exposed, a suture-ligature is placed and the vein divided.
(4) A single tie is placed above the suture-ligature to prevent the blood from coming in contact with injured intima.
(5) This shows the femoral vein with ligated stump flush with the wall but not encroaching upon the lumen of the vein.

sclerosing solution at the time of operation; the cases, however, have not been followed a sufficient length of time for an accurate appraisal of its value.

(5) *Excision.*—A simple excision of varicose veins was performed without a high ligation in a small number of patients. The procedure was carried out below the knee in most instances.

(6) *Low Ligation.*—(Trendelenburg operation): The simple ligation of veins in the midthigh was occasionally used.

Analysis of Results.—In determining the results of the 178 operations upon 121 individuals, it was thought best to treat each extremity separately and to set up arbitrary standards. In almost every case the operation has been combined with injection, either before operation, to heal an ulcer, or after operation, to thrombose any varicose radicles.

The results are classified on the following basis:

(A) An excellent result—the patient is free of symptoms and without visible or palpable varicose veins. Ulcers are not present.

(B) A good result—the patient is free of symptoms, but with small varicosities which can readily be cared for by injection. Ulcers are not present.

(C) A fair result—there is improvement in the severity of the symptoms and evidence of varicose veins. Ulcers are not present.

(D) A poor result—there is no improvement in the severity of symptoms or in the size of the veins. An ulcer may or may not be present.

It will be noted in the above classification that a persistent or recurring ulcer immediately places the result in the category termed "poor." When there has been a question regarding results, the poorer classification has always been chosen.

RESULTS OF OPERATION

(1) *Simple High Ligation:* 59 operations. In this group there were 21 results considered excellent; 23 were good; 13 fair and 2 poor. In one case, rated as a poor result, the patient did not return for injections; in the other, the operation was not sufficiently extensive.

(2) *Simple High Ligation and Injection at the Time of Operation:* 14 operations. In this group of cases there were 9 results which were considered excellent and 5 good. There were no failures.

(3) *Simple High Ligation and Excision:* 88 operations. In this group there were 47 results which were considered excellent; 30 good; 6 fair and 5 poor. The various causes of the poor results were apparently inadequate excision, poor selection of procedure, and disregard of evident contraindications to operation.

(4) *High and Low Ligation:* 4 operations. The results were classified as excellent in 2; good in 1, and fair in 1. None of this group was considered a poor result.

(5) *Simple Excision of Varicose Veins:* 8 operations. Although only a small number of cases were subjected to this form of treatment, it carried a high percentage of poor results. Two of the 8 cases were considered excellent; 1 good, 1 fair and 4 poor. In all of the 4 poor results, failure was due to inadequate surgery.

(6) *Low Ligation:* 5 operations. The results prove the futility of this procedure. None was considered excellent, none good, 3 fair and 2 poor.

Again the patients with poor results were found to have had inadequate procedures.

SUMMARY OF CASES

When the 178 operations for varicose veins are combined, it will be seen that the results, irrespective of method used, were excellent in 81, good in 60, fair in 24 and poor in 13 cases. This summary is shown in Chart 1.

TYPE OF OPERATION	TOTAL NUMBER	END-RESULTS							
		EXCELLENT		GOOD		FAIR		POOR	
		NO.	%	NO.	%	NO.	%	NO.	%
HIGH LIGATION	59	21	36	23	39	13	22	2	3
LIGATION AND INJECTION	14	9	74	5	39	0	0	0	0
LIGATION AND EXCISION	88	47	53	30	34	6	7	5	6
HIGH AND LOW LIGATION	4	2	50	1	25	1	25	0	0
EXCISION	8	2	25	1	12.5	1	12.5	4	50
LOW LIGATION	5	0	0	0	0	3	60	2	40
TOTAL	178	81	45	60	35	24	13	13	7

CHART 1.—Showing the total cases for each type of operation, and the end-results.

If the cases treated by excision (8) and low ligation (5) are excluded from the total—and these procedures should be condemned save in very exceptional cases—there remain 165 operations with excellent or good results in 138, or 84 per cent. In only seven cases was the result poor; therefore, in only 4 per cent was there no improvement in symptoms.

TYPE OF OPERATION	DURATION OF FOLLOW-UP PERIOD								TOTAL
	1 YEAR	1 1/2 YEARS	2 YEARS	2 1/2 YEARS	3 YEARS	4 YEARS	5 YEARS	6 YEARS	
HIGH LIGATION	13	18	16	6	5	1	0	0	59
LIGATION AND INJECTION	2	4	4	0	2	2	0	0	14
LIGATION AND EXCISION	19	19	15	12	11	9	2	2	88
HIGH AND LOW LIGATION	1	0	2	0	0	0	0	1	4
EXCISION	2	2	1	1	0	2	0	0	8
LOW LIGATION	1	0	0	0	4	0	0	0	5
TOTAL	38	43	38	19	21	14	2	3	178
PERCENT	21	24	21	11	12	8	1	2	

CHART 2.—The duration of follow-up; cases grouped according to the length of follow-up.

The analysis of cases was carried further to show—in each case—the period of time elapsing since operation. The results of this study are shown in Chart 2, in which the cases are grouped according to the operative procedure and the length of follow-up. The average length of postoperative observation was 2.1 years, and all cases were followed for at least one year.

Although the number of cases is too small to permit definite conclusions, each follow-up period is recorded according to the operative procedure and again subdivided according to the end-results. This is shown in Chart 3. There is little change in the comparative results from year to year.

An attempt was made to follow each patient from year to year in order to ascertain at which time a result might be considered permanent. In this study we were unsuccessful due to the irregularity of the time of follow-up visits and to change in examiners. It is our opinion, however, that poor results usually become evident one year from the time of operation.

In the total series of cases there were three instances of pulmonary emboli after operation, two of which terminated fatally. Both deaths occurred after a high ligation and excision. In reviewing these three histories, several factors of interest were noted: The patients were kept in bed some time after operation; the ligation of the saphenous vein was not flush with the femoral

vein in at least two cases; adequate exposure may have been sacrificed by omitting a third assistant at the operating table.

SUMMARY.—One hundred and sixty-nine patients, treated at the New York Hospital for varicose veins during seven years have been reviewed, with comments on certain clinical aspects. A description is given of the six types of operation employed in the treatment of varicose veins in this and other clinics, and the end-results compiled to show the comparative value of these various procedures. A comment is made on the cases which were considered failures.

VARICOSE VEINS.

TOTAL NUMBER — EXCELLENT | GOOD | FAIR | POOR

| TYPE OF OPERATION | DURATION OF POST-OPERATIVE FOLLOW-UP AND RESULTS | | |

high ligation of the internal saphenous vein, with injection of sclerosing fluid at the time of operation.

(5) Any modification of operative procedure answers the requirement so long as the ligation of the saphenous vein is carried out at the saphenofemoral junction, and the tributaries in this region are divided. An operative procedure must be chosen which most nearly corrects the faulty vascular system in the individual case.

(6) If the perforators or valves of the saphenous vein are incompetent, operation followed by injections of sclerosing fluids offers the best chance of a permanent cure.

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THE PROBLEM OF CATGUT SENSITIVITY AND ITS RELATION TO WOUND HEALING*

A PRELIMINARY REPORT

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EXPERIENCE with thoracoplasty wounds closed with catgut brings out the fact that healing is very frequently poor. Although such wounds are probably the most abused of surgical incisions, this factor alone does not seem to be an adequate explanation for the disappointing results obtained.

The suture material employed was singled out as one probable responsible factor because when silk was used throughout all stages, healing was very satisfactory. Thus, abuse of the wound by frequent reopening could be minimized in its importance and the suture material employed, emphasized.

The possibility of sensitization to the suture material was suggested because the instances of poor healing appeared to occur with surprising regularity during the earlier stages. The later stages all seemed to heal kindly.

Reviewing the literature failed to reveal convincing evidence that sensitization to catgut did or did not occur, and, therefore, elucidation of this point seemed highly desirable.

The Wound.—The commonly employed posterolateral thoracoplasty wound is one of the largest wounds surgically produced, and the principal adverse factors which undoubtedly affect it can be summarized as follows:

(1) The parascapular mass of muscle is thick and narrow, reducing thereby its elasticity, and more directly transmitting tension as result of shoulder motion to the suture line.

(2) The jutting ledge formed by the uppermost unresected rib produces distortion in the wound of varying degrees.

(3) Excessive accumulations of fluid within the extrapleural subscapular space will tend to point at the weakest place in the extracostal wall, namely, the incision.

(4) The blood supply to the lateral flap of the incision is compromised by being transected at approximately right angles to its axis of supply. Some compensation is had from anastomotic sources, but the middle third of the wound is the farthest from such an additional source. The middle third of the wound can be considered on this basis the danger zone of the incision.

(5) Reopening of the wound in approximately three weeks, recurrently, is probably the greatest single direct insult.

The closure of such wounds in the cases to be considered is routinely with catgut, using size No. 00 for the deep muscle layer in a continuous stitch through-and-through the muscle mass, being interrupted, however, at several points. Size No. 000 catgut is very frequently used in a superficial layer,

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including the superficial fascia and subcutaneous tissues. This is not always used but is employed in the majority of cases. It is uniformly a strictly interrupted layer. The skin is closed with interrupted black silk. Closures are occasionally affected by placing small interrupted catgut sutures in the fascial plane, using a multilayered, small bite, interrupted technic.

Occasionally, silk is used throughout, in which case the usual technic is observed, making a multilayered, small bite, interrupted closure. Comparison of these three types of closure offers a very interesting study. Uniformly, all of the wounds closed with silk, when reopened, present a remarkable restitution to normal of the fascial and muscular layers. The tissues are dry and the areolar planes are very easy to find, being well preserved. In contrast, the wounds closed by the more common method of bulk suturing of the muscle layers with catgut presents a widespread obliteration of all areolar planes within at least one inch of the original incision, and the tissues are replaced by edematous scar. Intermediate between these two extremes lies the wound closed by interrupted catgut. Here the fascial planes are fairly well preserved because of their more accurate approximation, but the edematous scar and obliteration of the areolar spaces is quite marked. These wounds are all, at the time of being reopened, approximately three weeks old.

The catgut used is put up in standard sizes. Its method of preparation is the usual one, except that it is iodized and tanned to insure sterility and to increase its persistence in the wound. The amounts actually left in the wound have been determined by carefully measuring all the loose pieces remaining after operation and subtracting this from the original lengths broken for the procedure. The figures thus obtained show that between 129 and 162 inches are actually left in the wound. An average figure would be 140 inches, or slightly more than the content of two tubes. This amount of catgut would weigh approximately 0.6 Gr.

Present Study.—As suggested by the literature,[3, 5] though after several unsuccessful attempts, an extract of plain catgut was made in Coca's solution by the following method: Two and one-half grams of plain (iodized but untanned) sterile catgut was thoroughly dried in an oven. This was then extracted in sterile Coca's solution for 48 hours, with agitation. The resultant mixture was passed through a Seitz filter. The solution was sealed in serum bottles and cultured to determine sterility.

Chemical analysis of this extract revealed 69.5 mg. per cent total nitrogen, and 1003.3 mg. per cent of iodine.

This extract seemed to give reliable results under adequately controlled conditions.

All patients admitted for thoracoplasty were subjected to the skin test and the results recorded. Following each stage, approximately two weeks postoperatively, the skin test was repeated. A total of 54 patients passing through the Service had a total of 113 skin tests. Distribution of the skin tests according to stages is given, and the results are presented in Chart 1 by Curves 1 and 2.

This extract is injected intradermally in 0.02 cc. amounts, and each test is

controlled by a similar amount of plain Coca's solution injected intradermally in a nearby area. The reactions are read in 15–20 minutes and graded in the usual manner. The reactions are usually faded by 45 minutes, leaving, in cases of severe reaction, a small area of brown discoloration.

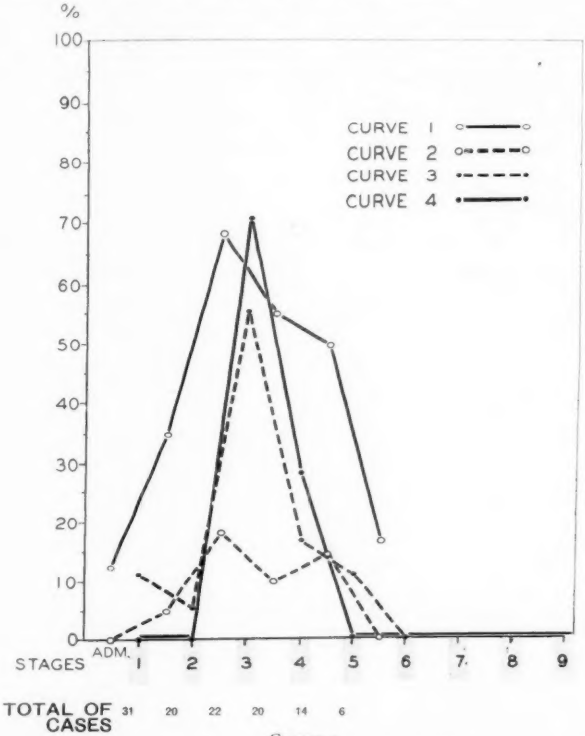

CHART 1.

Curve 1—Represents percentage-incidence of skin tests positive in any degree, by stages of thoracoplasty.

Curve 2—Represents percentage-incidence of highly positive skin tests by stages.

Curve 3—Represents percentage-incidence of all wound complications, by stages.

Curve 4—Represents percentage-incidence of wound complications exclusive of infections, by stages.

Reference to the chart reveals the graphic representation of the skin tests. Curve 1 represents the percentage of reactions positive in any degree, among the patients tested at each period in the evolution of the thoracoplasty. Curve 2 represents the percentage of reactions that were highly positive at the same periods. Thus, on admission some 12 per cent of patients tested showed evidence of skin sensitivity but none of them reacted strongly.

The peak of sensitivity as estimated by the skin test, therefore, occurs after two stages of thoracoplasty or, in other words, after two exposures to catgut. Thereafter, the sensitivity fluctuates but returns to the original level after the fifth dose.

Curve 2, although necessarily low, is quite comparable to Curve 1.

The intensity of the response to the skin test was carefully compared to the severity of the inflammatory reaction in the next-stage wound and a surprisingly accurate prediction of the appearance of the wound could be made, it was

found, on the basis of the preoperative skin test. Thus, the severity of the apparent inflammatory reaction in the wound accurately paralleled the intensity of response to the skin test preoperatively.

A wound presenting a characteristically severe reaction is worthy of description. This could be seen as early as the beginning of the second postoperative day. Two features were present and will be described separately.

The first to become noticeable is redness along the wound margin. By the fourth and fifth postoperative days, this has extended to involve an area one to one and one-half inches around the wound. By this time the discoloration has assumed a brawny tint. By the sixth and seventh days the color is beginning to fade and desquamation may be seen. This takes place as small branny flakes. The reaction has largely subsided by the tenth postoperative day.

Shortly after the appearance of the redness, the presence of edema can be noted. This starts in the wound margins and extends, increasing in amount, until about the fifth or sixth day. At this time it may extend from the spine posteriorly well into the axilla anteriorly. The wound itself is moist, weeping, and its edges are rolled up, resulting in poor apposition. The edema subsides rather rapidly after the seventh day and has disappeared entirely by the tenth day.

After the reaction has subsided, the wound invariably presents considerable scabbing. The wound edges are irregularly apposed. The resulting scar is broad and irregular.

The foregoing description is, of course, the severest form observed. All grades of severity may be seen, and the mild reactions undoubtedly represent merely the exudative response to an absorbable suture material and must be considered as essentially normal.

Careful observation of these wounds revealed that the severest reaction any patient presented was regularly in the third-stage wound. This, of course, depends upon simple inspection and may be subject to error.

The wound complication that appears to be a direct sequela to this wound reaction resolves itself into a separation of the wound edges when some of the sutures, usually alternate ones, are removed. This separation most frequently occurs in the middle third of the wound where stress is probably greatest. The linear extent of this separation is determined by the distance left unprotected by the removed sutures. Such disruption permits escape of fluid from the subscapular extrapleural space, indicating separation of the muscle layers as well as the skin. This incident most often occurs at the fifth day, when one-half of the sutures are routinely removed.

One other observation on the behavior of such wounds has been that patients presenting mild skin sensitivity only, have been subject to exactly this complication. This fact appears at first to be somewhat contradictory. The answer is, however, readily forthcoming from the work of Kahn,[4] who showed that various tissues of the body had different capabilities of reacting to antigens introduced into them. Thus, it has been observed that the extent of reaction exhibited by the muscle layers, as evidenced by widespread edematous, cicatricial obliteration of the areolar and fascial planes when a wound is opened

at a thoracoplasty-stage, is not always commensurate with the degree of skin sensitivity as measured by the skin test reaction. Thus, whereas the skin test mirrors very accurately the reaction to be seen in the skin and probably subcutaneous tissues at the succeeding stage, it does not necessarily reflect the extent of reaction in the muscle tissues.

Thus, at this point the practical value of the skin test decreases because while it will predict the appearance of the wound postoperatively, it may not foretell the extent of underlying reaction. It is believed that this underlying reaction is, from a practical standpoint, far more important than mere skin sensitivity or reaction. This fact makes any estimate of the percentage accuracy of the skin test a matter of speculation.

The amount of reaction manifested by the skin can only be regarded as a measure of the ability of this layer to respond as a reacting system and not as a measure of the capability of the organism as a whole or any other specific tissue in particular.

The fact that the skin reacts as a unit system is demonstrated by the finding that reaction to the skin test is the same near the wound as it is at a distance from it.

This fact is further strengthened by the following observations:

(1) Using blood serum from patients presenting severe wound reactions, as well as four plus skin test reactions, passive transfer of antibodies was attempted in six different subjects. In no instance could such an occurrence be demonstrated.

(2) Using the extract as antigen, precipitins could not be demonstrated in the blood serum of these same patients.

(3) Using serum obtained from the extrapleural space of numerous patients, again, precipitins could not be demonstrated.

An explanation was sought for this apparent insecurity of catgut wounds in patients exhibiting marked sensitivity. Although the data herein presented is fragmentary because of fear that sinuses might be produced by any elaborate experimentation with these wounds, nevertheless an answer is suggested by the following experiment: A silk thread was securely tied around one of the subcutaneous catgut sutures in three first-stage wounds in nonsensitive patients. Lysis of the catgut, as indicated by freeing of the silk thread, occurred on the tenth day in one instance and on the twelfth day in the other two. In a patient exhibiting mild sensitivity at the end of the second stage, a similar experiment revealed the catgut thread in the third-stage wound to break at a slight tug on the sixth day. In a highly sensitive patient whose wound was opened by the sixth postoperative day, no evidence of remaining catgut was seen.

Thus, it would seem that in the presence of an hypersensitive response, lysis of the catgut sutures occurs with greater rapidity than in normal individuals.

Incidence of Wound Complications.—The analysis of reactions seen in wounds is difficult because it is quite impossible to accurately weigh the proportionate responsibility of the many factors concerned in the healing of

wounds. In order to eliminate, therefore, the factor of personal interpretation, the records of all thoracoplasties, unselectedly, were reviewed for approximately six months. This included some patients prior to the institution of this study and does not include all patients who were skin tested. It represents a comparable group, insofar as technic, surgeons, and care are concerned.

No attempt was made to classify the various complications except to call wound infections those instances where the wounds were opened for drainage and pyogenic organisms were recovered by culture. The infecting organism was a *Staphylococcus aureus* or the tubercle bacillus in every instance. Two instances of tuberculous infection of these wounds are included.

In this group there were included, of course, several patients who had had previous stages of thoracoplasty prior to this admission. In such instances, the old records were reviewed and complications tabulated. Thus, 45 patients underwent a total of 184 stages of thoracoplasty.

Complications were recorded in 18 instances, or an incidence of 9.7 per cent. Eliminating the frank wound infections, of which there were 11, or 5.9 per cent, leaves seven, or 3.8 per cent of complications of other types. Four instances in this latter group of complications came under direct observation in this study and corresponded to the previously described reaction to catgut.

This data can be graphically represented by Curves 3 and 4 of Chart 1. Curve 3 represents the percentage of all complications occurring at each stage. Thus, it includes frank wound infections as well as those presenting only separation of the skin edges and leakage of extrapleural fluid. Curve 4 represents the percentage of the complications exclusive of the infections occurring at each stage.

When all complications are considered (Curve 3), the curve produced very closely parallels the curve of skin sensitivity (Curve 1). No complications were encountered after the fifth stage, and there was a total of 12 operations beyond this stage. The high level at the first stage is in all probability accidental, being due to the rather unusual occurrence of infection in first-stage wounds within this group of patients.

The striking feature in both of these curves is the fact that the peak of incidence for wound complications of any sort occurs in the third-stage wound, which represents the inoculation of catgut immediately following the peak of sensitivity as demonstrated by the skin test.

SUMMARY AND CONCLUSIONS

Evidence has been presented that:

(1) Sensitivity to catgut, used in rather large doses and repeatedly, can be demonstrated by means of a skin test.

(2) The curve of the sensitivity closely corresponds to the immunologic response to the commonly used antigens.

(3) It is intimated that in sensitized individuals, lysis of the suture material occurs more rapidly than in the nonsensitized person.

(4) The reacting capacity of different fundamental tissues varies. It is further suggested that although most often the skin is capable of greater

reaction than skeletal muscle and/or its fasciae, in some individuals even this relationship may be variable. It is believed that the reaction in the muscle layers is more important from a practical standpoint than that of the skin alone.

(5) The sensitization to catgut appears to be a purely local reaction, confined to the tissues as a reacting system since no evidence of systemic response has been seen.

(6) When the wound complications occur, they do so with amazing frequency at a period in the evolution of the thoracoplasty when sensitivity is highest, as demonstrated by skin tests.

It is believed that, insofar as wound complications are concerned, the only one that can be attributed to hypersensitivity to catgut is the result of a delay in the process of healing. Apparently, the first reaction to catgut is inflammatory, producing the redness and edema described. The result of this is early lysis of the suture material. The fibroblastic reaction is apparently delayed until this exudative reaction has subsided. Thus, it would be an intensification of the usual exudative reaction to catgut.

Some accessory factor, such as loss of support by removal of skin sutures or mechanical stress exerted by the scapula, is believed to precipitate such an occurrence. It can be averted by maintaining apposition of the skin edges for ten days, at which time healing should be fairly well advanced.

(7) The exact component of a catgut suture which acts as an antigen cannot be determined from this study alone.

According to the Wolff-Eisner hypothesis,[6] the iodine present in the catgut could become antigenic by combining with serum in the wound. Jacobs[2] has shown that serum tends to lose its species specificity after iodinization. It might further be in the iodine-catgut protein combination, or actually the catgut protein itself.

Rather conclusive evidence, however, has been brought out by Farris[1] that it is the protein itself. He obtained a very severe intra-occular reaction around catgut in rabbits after sensitization of these animals to sheep serum. Such reaction did not occur in nonsensitized animals.

(8) The skin test has no practical significance in sorting suitable candidates for catgut closures because it is often only after one or two stages that sensitivity becomes demonstrable.

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THE RÔLE OF THE LIVER IN PREOPERATIVE CARE

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INTELLIGENT PREPARATION of the surgical patient requires an appreciation of varied physiologic principles. Although it may be desirable, it is difficult to formulate rules applying in all circumstances. Diseases and patients vary too much and fixed rules do not allow for the prompt application of new findings by chemists and physiologists. Preoperative care must, insofar as is possible, repair the damage to the whole organism which has been brought about as a result of disease. This concerns nutrition, water and salt balance, adequate oxygenation, and such matters. The patient must also be fortified to withstand the operative measures necessary for radical control of the disease. He must be able to destroy the anesthetic agent which is used, to compensate for the loss of blood and fluids which even the gentlest handling will bring about, and to withstand the effects of a period of shock. There must be a reserve sufficient to supply the needs of the body during the postoperative period when adjustments to metabolic disturbances must be made and when ordinary methods of providing nourishment have been suspended. In this era of generally good technical ability, the improvement in morbidity and mortality statistics depends more on the intelligent application of such measures than on improvements in technic. The limit of advance is our ability to maintain the patient's good condition during long procedures. Anesthesia has extended its possibilities; it remains for attention to details of preoperative care to extend the limits.

Knowledge of the physiology of the liver is essential for the understanding of many principles involved in preoperative care. It is the one organ in which many of the processes take place. Our information about its function is meager; but not so lacking as to justify an attitude of hopelessness. Too often, one hears there is no one satisfactory liver function test, with the implication that all tests may be disregarded.

There are many highly satisfactory methods of evaluating the ability of the liver to do its job. A consideration of its various known functions and methods of testing, restoring, or increasing those functions will be made. Particular stress will be laid on the more recent additions to our knowledge and to significant experimental work.

Blood Clotting.—The liver is the site of the manufacture of the fibrinogen fraction of the plasma protein[1]—normally, the serum contains about 250 mg. per 100 cc. Fibrinogen is the soluble precursor of the insoluble fibrin in the clot. The serum content of this protein varies under different circumstances,

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apparently independently of the leukocyte count. It is elevated, among other factors, by abscess formation, moderate liver damage,[2] foreign protein injections, and fever; and decreased by severe liver damage and protein-deficient diet. The sedimentation rate of red cells is a rough index of the fibrinogen level, accelerating as the protein concentration increases.[2a] Much work remains to be done on this protein. Its value as a test of the state of the liver or the ability to respond to blood-clotting demands has never been fully appreciated.

The liver is also the site of the manufacture of prothrombin. It is made from unknown substances, and is dependent on an adequate supply of vitamin K or some substance with vitamin K activity. With thromboplastin and calcium, prothrombin forms thrombin. Its level in the blood is easily determined by one of several methods. The absorption of vitamin K by the gastrointestinal tract is in combination with deoxycholic acid;[3] obstruction to biliary flow, therefore, will prevent this absorption and the prothrombin deficiency is the cause of bleeding in jaundice.[4] In severe damage to the liver that organ is unable to manufacture prothrombin, in spite of adequate supply of vitamin K or a substance with vitamin K activity.[5]

Heparin was first prepared from the liver by Howell but it has since been obtained from many other organs, notably the lung and intestinal mucosa. Its manufacture is in some way linked to the mast cells present in large numbers in the smaller blood vessels.[6] It is stored to some extent in the liver.[7] The prevention of thrombosis in the postoperative period is dependent on an adequate supply of heparin for the serum. The delicate balance between the coagulants and heparin, the body's anticoagulant, is important. The liver has a large measure of control over this balance. Disorders are rather an excess of clotting factors than a deficiency of heparin and the imbalance may be met by the administration of additional heparin.[8] There is no known method for stimulating the production of heparin.

Detoxification.—One of the earliest known functions of the liver is that by which it destroys noxious substances which enter the body. It has been known that any condition which interferes with the liver's ability to destroy poisons will produce rapidly disastrous effects. Studies of this function have generally been concerned with methods of rendering the liver susceptible to damage. Opie and Alford,[9] in 1914, showed that a high fat diet would ultimately render the liver unable to withstand the administration of chloroform. This will be referred to later in a consideration of fatty liver. Ravdin and his coworkers[10] have studied the influence of foodstuffs on the susceptibility of liver to injury and with many other workers have demonstrated that starvation and low glycogen content of the liver may bring about this susceptibility. Tests for the detoxification properties commonly used are the bromsulphalein and the tetraiodophenolphthalein blood clearances—simple measurements of the ability of the liver to withdraw these easily detectable dyes from the blood during a certain time-interval. Another test which has been designated by some as a test of the detoxifying property of the liver is the hippuric acid

synthesis test of Quick. This test is a measure of the ability of the liver to conjugate benzoic acid with glycine to produce hippuric acid which is excreted in the urine. It depends upon a satisfactory renal function. The test may measure another function of the liver, namely, its ability to manufacture the amino-acid, glycine, because the addition of glycine to the benzoic acid will produce a normal synthesis in the presence of parenchymatous disease of the liver.[11] The detoxifying property of the liver may be improved or restored by reestablishing a high glycogen content. A discussion of this topic involves the function of the storage of glycogen.

Storage of Glycogen.—The storage of carbohydrates in the form of glycogen, the manufacture of dextrose from proteins and fats, and the maintenance of blood sugar level are functions of the liver. The level of glucose in blood represents a balance between the rate of supply from the liver stores and the rate of utilization by tissues other than the liver. The so-called normal sugar tolerance curve has no relation to the function of the pancreas. The liver is the only source of blood sugar in a fasting organism.[12] This function of the liver is tested by either levulose or galactose tolerance tests. In the presence of liver damage the slow return and elevation of the curve are characteristic. In ordinary circumstances the glycogen content of the liver can be elevated by high carbohydrate diet. In the absence of ability to take food by mouth this may be accomplished by glucose infusions into the blood stream. There are conditions when an infusion or carbohydrate ingestion will not build up the glycogen stores of the liver. They will be discussed later.

Storage of Protein.—The normal seven grams per 100 cc. of plasma protein is divided into large heterogeneous groups by chemical salting into albumin and globulin fractions. The manufacture of fibrinogen which is part of the globulin has been discussed. Of the remaining plasma protein, probably all the albumin fraction, and some of the globulins are manufactured in the liver. The importance of adequate supplies of proteins need not be emphasized to a surgical group. The treatment and prevention of shock and proper wound healing are directly dependent on an adequate plasma protein level and a normal partition. In deficiencies of the liver affecting its ability to manufacture the albumin fraction, the ratio between albumin and globulin is disturbed. The albumin is known to maintain the greatest part of intraluminary osmotic pressure, the globulins exerting only one-fifth of the total attraction while taking almost one-third the total bulk. The edema from loss of albumin, then, is greater than would be expected from the proportion of total protein which is lost. It is this edema which interferes with wound healing in patients with gastro-intestinal diseases not supplied with proper protein intake before operation. The ability of the liver to supply serum albumin in sudden shifts of osmotic pressure is one great factor in combatting shock. The tests for protein deficiencies in the liver are serum albumin and globulin determinations. The total proteins in serum may be determined very easily by modern specific gravity methods. To restore sufficient proteins any one of a number of measures may be used. The most direct and quickest is the transfusion of

human plasma, and for osmotic pressure the most useful fraction is the albumin. This is necessary in the emergencies where a large amount of serum has been lost, such as in burns. In most circumstances a high protein diet will be sufficient to restore the protein. Elman[13] has demonstrated that in patients who are unable to ingest a high protein diet, highly purified amino-acids may be used intravenously.

Bile Acid Conjugation and Circulation.—Normally, the liver manufactures the bile acids by conjugating choleic acid and the amino-acids, glycine, and taurine. The source of the choleic acid is not entirely clear but the liver is almost certainly the site of manufacture. These bile acids form a very necessary function in the absorption of fats in the gastro-intestinal tract. The formation of choleic acid takes place in the intestinal mucosa but is dissociated before the fat is taken up by the lymph. The bile acids may thus serve to transport a considerable quantity of fat. On release the bile acid enters the blood stream directly; it does not traverse the thoracic duct with the fat. Through the portal vein to the liver, where it is secreted again, the circulation is maintained.[14] This circulation cycle in man occurs about three times; the loss is through the feces. The sudden total drainage through biliary fistulae or the interference with circulation which biliary obstruction produces taxes the ability of the liver to conjugate more acids. The uniformly low rate of hippuric acid synthesis in this group of patients would indicate a shortage of glycine which is necessary for the conjugation of both hippuric acid and glycocolic acid. The restoration of the hippuric acid by the administration of glycine or glycine-containing products is probably an indication that bile acid production has been resumed.[11] That some degree of circulation takes place in obstructive jaundice is shown by Shafiroff, Doubilet, and Ruggiero.[15] In a dog with an obstructed common duct, bile pigment may be found in the thoracic duct within ten to 20 minutes after obstruction occurs.

Josephson[14] has suggested a liver function test on the basis of the ability of the liver to clear the blood of injected cholate. Other tests of this function of the liver are analysis of the bile for free and conjugated acids, and blood levels of bile acids. Normally, most of the bile acids are conjugated with glycine or taurine. The occurrence of large quantities of unconjugated acids may be considered an evidence of liver damage. As in the conjugation of hippuric acid, glycine is an important material in the formation of normal bile acids. Restoration of normal function should be brought about by feeding of proteins with high glycine content. The bile acid formation and circulation seems to be entirely independent of other liver functions.

Storage of Fat.—There has been a great deal of recent work reported by chemists and physiologists on the fat-storing property of the liver. Normally, 6 per cent by weight of the liver is stored fat. A propensity of the organ to store fat in concentrations higher than this is a definite pathologic condition. It has been known, since the work of Opie and Alford,[9] in 1914, that such fatty infiltration renders the liver more susceptible to injury by chloro-

form and other toxic agents. Since 1922, and the use of insulin, the knowledge that in depancreatized dogs fatty liver follows, and this fatty liver may be prevented or cured by the feeding of raw pancreas,[16] has stimulated many studies. We know now that fatty liver may be produced by starvation,[10] high fat diet,[9] common bile duct obstruction,[17] vitamin B_1 and B_6 deficiencies,[18] alcohol, chloroform, and many other factors. In the presence of large amounts of fat, the liver is rendered unable to store glycogen,[10] to manufacture dextrose, to excrete dyes,[19] and will, according to Connor,[18] eventually produce cirrhosis of the liver.

Hershey and Soskin,[20] in 1932, showed that substances other than raw pancreas (the phospholipids, lecithin and cephalin) will prevent fatty infiltration. Since then many other materials have been demonstrated to have this lipotropic effect: choline, egg albumin, casein, gelatin and, finally, the sulphur-containing amino-acid, methionine. Dragstedt[21] has reported the finding of a hormone in the external secretion of the pancreas, which he calls lipocaic, that has a lipotropic action. Ralli and Rubin[22] have reported that an extract removed from powdered meat, when added to a depancreatized dog's diet, produces fatty liver, whereas the powdered meat alone has no such effect.

Ravdin,[10] in animal experiments, has shown that the liver may contain large quantities of fat and glycogen at the same time. The high glycogen content in such circumstances is no longer protective against injury by chloroform. The susceptibility is related only to the fat content. The protective action of glycogen in most instances is due to the fact that high glycogen indicates the absence of fat. In order to replace the fat, a lipotropic substance must be fed. Glucose alone is not sufficient. The most convenient and speedy method of supplying the lipotrope is by a high protein diet. Although Elman[13] has demonstrated that nitrogen balance may be maintained by the intravenous administration of amino-acids, the preparation of such solutions is difficult and expensive.

Unfortunately, there is no test for the presence of fat in the liver. In large quantities it will interfere with the ability of the organ to perform many of its functions and will make it more susceptible to the effects of toxic substances. There is one clinical finding which is helpful. A liver which contains 10 per cent by weight of fat will generally be enlarged appréciably. The enlargement is the characteristic painless, smooth, round edge found in chronic alcoholics. It would seem that the measures which correct fatty liver might be applied to all patients without harm and particularly to those whose liver function will be taxed by a long and shocking operative procedure.

Pathologic changes in the liver, not related to a known function, have engaged the attention of many workers. The clinical similarity of the syndrome called "liver death" and thyroid crisis has been noted by clinicians. Boyce and McFetridge[23] remarked this similarity, and found with hippuric acid synthesis tests that thyroid disease disturbed the function of the liver in direct ratio with the disease clinical severity. Schmidt and his coworkers[24]

feel that the liver damage is related to the duration and severity of the disease and that specific measures to correct the damage, glycine administration for instance, will lessen the risk. They also feel that the operation of thyroidectomy has a damaging influence on liver function. Bartels,[25] expressing the feeling of the Lahey Clinic group, feels that the liver changes are directly due to the thyroid disease and are the pathologic factors in thyroid crisis. Experimentally, there seems to be evidence that another factor must be added to the hyperthyroidism to produce the characteristic central liver necrosis. Sealy[26] has induced the liver changes in rabbits when an infected warty growth of the skin was present at the time of the production of hyperthyroidism. He infers that the clinical occurrence of liver necrosis may be dependent on some added factor such as infection or anesthesia.

Other effects of feeding of specific proteins on liver should be noted. Mori[27] found that adding protein in the form of kidney feedings to a rice diet will protect rats from the carcinogenic effect of butter yellow on the liver. Rhoads and a group[28] at the Memorial Hospital have shown that casein and riboflavin supplements to a basil diet have a striking protective effect against the same carcinogen in rats.

There are tests of liver damage which have no relation to function and which parallel no function test. One of these has become especially valuable and should be mentioned. Hanger[29] described the peculiar property of serum from a patient with parenchymatous liver disease to flocculate a suspension of cephalin in cholesterol. This test is not only valuable for diagnosing liver damage but is also helpful in differentiating obstructive from hepatogenous jaundice.

To summarize, certain aspects of the physiology of the liver as it is related to the problems of preoperative surgical care have been reviewed. Some of the more recent contributions of the chemistry laboratories have been considered in the light of clinical needs.

There is definite evidence that the liver can be fortified against injury or impairment of its functions by specific measures. The feeding of glycine in pure form or in a protein diet will bring about a normal ability on the part of the liver to conjugate hippuric acid from sodium benzoate and probably to conjugate glycocholic acid from cholic acid. The feeding of a high protein diet and perhaps some substances, lipocaic or choline, will promote the removal of fat from a fatty liver or prevent the deposition of fat under conditions which ordinarily produce the changes. There is convincing evidence that fatty liver is not only more susceptible to damage but may be a factor in the etiology of such conditions as thyroid crisis.

The liver's control over blood sugar levels, over plasma proteins, over bile acid manufacture and secretion, and its part in the complex mechanism of blood clotting and detoxification, have been considered. Many of the latest additions to our knowledge are in the animal stage. It remains for clinical surgeons to confirm or deny the application of these findings in the human.

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BRIEF COMMUNICATION

THE ADVANTAGES OF COMBINING LOCAL INFILTRATION ANESTHESIA WITH CONTROLLED FRACTIONAL SPINAL ANESTHESIA IN SUBSTANDARD SURGICAL RISKS

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OCCASIONALLY, in the practice of most surgeons, celiotomy must be performed upon patients who are bad risks for any type of anesthesia. When the character of and the site where the proposed procedure is to be carried out is accurately known, it is usually possible to employ local anesthesia, which most physicians agree entails the least risk for the patient.

Unfortunately, it is sometimes impossible to arrive at an exact diagnosis preoperatively and there are other cases in which one can feel reasonably certain of the diagnosis but in which the possibility of error persists. In such situations, and in bad risk patients, one is confronted with the following dilemma: On the one hand spinal anesthesia may be employed which will provide adequate exposure for whatever is encountered but entail considerable risk for patients with impaired circulation. On the other hand, local anesthesia may be used which will too frequently have to be supplemented with an inhalation anesthetic if the exposure and relaxation are not adequate. This often means a deep ether anesthesia with a difficult induction after the peritoneum is opened.

The use of Lemmon's apparatus for controlled fractional spinal anesthesia makes it possible to avoid this dilemma. The spinal puncture is done, the point of the needle left in place within the subarachnoid space, and the other end connected by rubber tubing to a syringe containing 500 mg. of procaine hydrochloride dissolved in 10 cc. of spinal fluid. However, none of this solution is administered at once. Instead the operation is begun under local anesthesia, exposing the patient to the minimum risk in opening the abdomen. After the abdomen is open, if the procedure indicated can be satisfactorily completed under local anesthesia, no spinal anesthesia is given. If, on the other hand, the necessary procedure requires extensive exploration or more relaxation, spinal anesthesia may be given in its safest form and maintained during such part of the procedure as is necessary. If it does cause a substantial drop in blood pressure and, this cannot always be avoided when the patients are on the verge of shock, the withdrawal of spinal fluid will usually shorten its action.

We have used continuous spinal anesthesia for nearly all abdominal cases, except appendicectomies, during the past 15 months. There have been no

table deaths, relaxation has been as perfect as with nupercaine, the anesthesia has been continued as long as four and a half hours, patients have been encountered who required several hundred milligrams of procaine hydrochloride, while others have been anesthetized to the costal margins with as little as 75 mg.

Thus, we have confirmed all the major claims of Lemmon for his method.

Although we have not employed the deferred method in a large group of cases, it has seemed to offer sufficient advantages in a limited field to warrant recommendation. Illustrative case records are summarized below.

The first two cases are those of patients, nearly moribund it is true, whom we dealt with before the use of controlled fractional spinal anesthesia. In one we chose the first horn of the dilemma and with the other we chose the other horn. Both patients died on the table.

The next is a patient in whom it was possible to omit the spinal anesthesia entirely, that is, the procedure was completed with local.

The last two required spinal anesthesia and small amounts were successfully administered during the critical stages of the procedure only.

Case 1.—A. R., Hospital of the University of Pennsylvania, #43581. Age 65, white, male, admitted 12–19–39.

The patient had meningovascular lues and tabes dorsalis. He also had cerebral arteriosclerosis with facial palsy and had recently had an anterior coronary occlusion.

At 4:00 P.M. he developed abdominal pain and on admission had a tender, resistant distended and silent abdomen. The preoperative diagnosis was peritonitis due to a ruptured viscus. Appendicitis with rupture at the base was considered most probable.

Operation.—A low spinal anesthesia was given by the single injection method but it was not very effective so the operation was begun with local anesthesia. The appendix was exposed through a McBurney incision. The peritoneal cavity contained large amounts of pus but the appendix was not ruptured. In order to explore the remainder of the abdomen general anesthesia was necessary. Cyclopropane and ether were used and a rupture was found in the sigmoid but the patient died on the table.

Case 2.—E. C. Graduate Hospital of the University of Pennsylvania, #146662. Age 45, colored, male, admitted 7–26–40.

The patient had had a ruptured duodenal ulcer 5–25–40 followed by evidence of a pelvic abscess which subsided without drainage. He was readmitted following vigorous catharsis with cramp-like pain, vomiting and a temperature of 102° F. Pulse rate was 130 and blood pressure 100/80. The abdomen was tense and distended. He was managed with suction drainage and supportive treatment for several days but finally the obstructive symptoms became definite and operation became necessary.

Operation.—Spinal anesthesia with nupercaine was employed. The relaxation was excellent. A distended loop of bowel was found and an enterostomy performed but the patient died on the table as the wound was being closed.

Case 3.—J. O'D. Graduate Hospital of the University of Pennsylvania, #149426. Age 36, white, male, admitted 1–30–41.

The patient was greatly overweight. He had been having precordial pain on exertion for five years and an electrocardiogram showed evidence of coronary disease. He had had indigestion for ten days and had moderately severe epigastric pain from 1:00 P.M. on 1–30–41. Maximum pain and tenderness were to the left. As they did not subside operation was decided upon the next day.

Operation.—A malleable needle was inserted in the back and connected by a tube

to a syringe containing 500 mgs. of procaine in 10 cc. of spinal fluid. Operation, however, was begun under local anesthesia. Acute cholecystitis and the edematous form of pancreatitis were found and cholecystostomy performed. No spinal anesthesia was necessary and none was given. The patient made a good recovery.

Case 4.—M. D. Pennsylvania Hospital, #58321. Age 65, white, female, admitted 4-6-41.

The patient had been treated for carcinoma of the cervix with radium in May, 1940. She had had diarrhea intermittently after that treatment and had been under the care of a cardiologist for attacks of auricular fibrillation. At the time of admission she had abdominal pain and vomiting; the abdomen was distended and tender. The patient was irrational and there were moist râles at both bases and some evidence of bronchopneumonia. The preoperative diagnosis was peritonitis and intestinal obstruction.

Operation.—Celiotomy was performed under local anesthesia and exploration and cecostomy under spinal anesthesia administered by our modification of the method described by Lemmon. Procaine was given at intervals of from five to 16 minutes. The successive doses were 25 mg., 25 mg., 12 mg., 12 mg., 12 mg., and 12 mg. The systolic blood pressure varied only between 120 and 108 Mm. of mercury. During the procedure 250 cc. of plasma was infused. The patient left the operating room in comparatively good condition.

Case 5.—A. M. Bryn Mawr Hospital. #1042170. Age 67, white, female, admitted 3-1-41.

The patient was admitted with signs of intestinal obstruction. She improved greatly after intubation with the Miller-Abbott tube and the obstruction was localized to the lower ileum. In spite of the improvement she continued to have a marked azotemia and râles at both lung bases. There was no history of coronary infarction but her physician did not believe that she had much cardiac reserve. She was quite obese.

Operation.—She was operated upon under local and controlled fractional spinal anesthesia. The abdomen was opened before any procaine was administered intrathecally. It was then found that the site of obstruction was deeply placed. Small doses of procaine were given and only then was it possible to expose and free an adhesion in the pelvis. The total amount of procaine given intrathecally was 75 mg. and this amount did not cause a serious drop in blood pressure.

CONCLUSIONS

Exploratory celiotomy is occasionally necessary in patients who are very poor operative risks.

The use of Lemmon's procedure for controlled fractional spinal anesthesia makes it possible to operate on these patients under local anesthesia and yet to switch to controlled spinal anesthesia if a condition is found which requires a greater exposure or more relaxation than the local affords.

We believe that this combination of anesthetic technics further reduces the combined dangers of anesthesia and intra-abdominal manipulation for this type of case.

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CORRESPONDENCE

To the Editor:

In an article entitled "Tumors of the Carotid Body," by S. W. Harrington, O. T. Clagett, and M. B. Dockerty, published in the November, 1941, issue of the Annals of Surgery, it is stated: (1) That the carotid bodies are homologous to the medullary portion of the adrenal medulla; and (2) that their function is negligible because bilateral extirpation may be performed without untoward symptoms.

Actually, the carotid bodies, together with the aortic body (a similar structure situated between the arch of the aorta and the pulmonary artery) are now known to have an unique and irreplaceable function because they contain sensory end-organs that respond to certain chemical changes in the arterial blood. These sensory receptors (now called chemoreceptors or chemoceptors) can be stimulated by a decrease in oxygen tension, or by an increase in CO_2 tension or acidity in the arterial blood, and by certain drugs and chemicals such as nicotine, lobeline, cyanide, sulfide, *etc.* The result of stimulation of these chemoreceptors is a marked increase in respiration and blood pressure; the afferent pathways are the two carotid sinus and two depressor nerves, entering the central nervous system by way of the glossopharyngeal and vagus nerves respectively.

The carotid bodies should be of particular interest to the surgeon for several reasons. First of all, it is now known that reflexes from these structures constitute the main defense of the body against anoxemia; the stimulation of the respiratory and vasomotor centers that occurs in periods of oxygen deficiency is certainly due preponderantly, and perhaps entirely, to carotid and aortic body reflexes. Lack of oxygen probably does not stimulate the medullary centers directly at all, as formerly believed; in fact, if the carotid and aortic bodies are denervated anoxemia becomes purely depressant to the vital centers and respiration and blood pressure, instead of increasing, rapidly fail. Fortunately, this chemoreceptor reflex system possesses a ruggedness which enables it to maintain respiration and circulation reflexly even though the medullary centers are severely depressed by such agencies as prolonged anoxemia and deep anesthesia.

It is true that bilateral extirpation of the carotid bodies may not lead to untoward symptoms, but this is due to the fact that the aortic body is never removed surgically and this structure can assume some or all of the functions of the carotid bodies. Even if the carotid *and* aortic bodies were removed, there probably would still be no outward signs of their absence until the organism was exposed to oxygen lack, in which case the vital functions would undergo steady and progressive deterioration without any stimulant phenomena whatever.

The original studies of carotid body function were made by C. Heymans, in Ghent, in 1931–1933, in recognition of which he was awarded the Nobel Prize in Physiology and Medicine in 1938. A number of review articles dealing with the functions of the carotid and aortic bodies have been published recently (Ergebnisse der Physiologie, 41, 28, 1939; Annual Review of Physiology, 1, 185, 1939; Physiological Reviews, 20, 115, 1940; Jour. Lab. and Clin. Med., 26, 223, 1940).

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